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**APPLICATION NUMBER: 60/579,342**

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# **U.S. PATENT AND TRADEMARK OFFICE PROVISIONAL APPLICATION FOR PATENT COVER SHEET**

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT  
under 37 C.F.R. §1.53(b)(2)

Atty. Docket: KOPCHICK15.1

INVENTOR(S)/APPLICANT(S)			
LAST NAME	FIRST NAME	MI	RESIDENCE (CITY AND EITHER STATE OR FOREIGN COUNTRY)
KOPCHICK	John	J.	Athens, Ohio
COSCHIGANO	Karen	T.	The Plains, Ohio
BOYCE	Keith	S.	Wexford, Pennsylvania
KRIETE	Andres		Pittsburgh, Pennsylvania

☐ Additional inventors are being named on separately numbered sheets attached hereto

**TITLE OF THE INVENTION (280 characters max)**

DIAGNOSIS OF HYPERINSULINEMIA AND TYPE II DIABETES AND PROTECTION AGAINST SAME BASED ON GENES DIFFERENTIALLY EXPRESSED IN MUSCLE CELLS (15.1)

**CORRESPONDENCE ADDRESS**

Direct all correspondence to the address associated with **Customer Number 001444**, which is presently:

BROWDY AND NEIMARK, P.L.L.C.  
624 Ninth Street, N.W., Suite 300  
Washington, D.C. 20001-5303

**ENCLOSED APPLICATION PARTS (check all that apply)**

<input checked="" type="checkbox"/> Specification	Number of Pages	293	<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 C.F.R. §1.27
<input checked="" type="checkbox"/> Drawing(s)	Number of Sheets	6	<input type="checkbox"/> Other (specify) _____
	Figures 1A-3B		

**METHOD OF PAYMENT (check one)**

☒ Credit Card Payment Form PTO-2038 is enclosed to cover the Provisional filing fee of

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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

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Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.

By:   
Iver P. Cooper

Registration No.: 28,005

Date: June 15, 2004

IPC: jlu

DIAGNOSIS OF HYPERINSULINEMIA AND TYPE II DIABETES AND  
PROTECTION AGAINST SAME BASED ON GENES DIFFERENTIALLY  
EXPRESSED IN MUSCLE CELLS (15.1)

*Cross-Reference to Related Applications*

5        *Anti-Aging Applications.* Mice with a disrupted growth  
hormone receptor/binding protein gene enjoy an increased  
lifespan. In U.S. Prov. Appl. 60/485,222, filed July 8,  
2003 (Kopchick8) mouse genes differentially expressed in  
10       comparisons of gene expression in growth hormone  
receptor/binding protein gene-disrupted mouse **livers** and  
normal mouse livers were identified, as were corresponding  
human genes and proteins. It was suggested that the human  
molecules, or antagonists thereof, could be used for  
15       protection against faster-than-normal biological aging, or  
to achieve slower-than-normal biological aging. It was also  
taught that the human molecules may also be used as markers  
of biological aging.

20       In provisional application Ser. No. 60/474,606, filed  
June 2, 2003 (our docket Kopchick7-USA) , our research group  
used a gene chip to study the genetic changes in the **liver**  
of C57Bl/6J mice that occur at frequent intervals of the  
aging process. Differential hybridization techniques were  
used to identify mouse genes that are differentially  
expressed in mice, depending upon their age. The level of  
25       gene expression of approximately 10,000 mouse genes (from  
the Amersham Codelink UniSet Mouse I Bioarray, product  
code: 300013) in the liver of mice with average ages of 35,  
49, 56, 77, 118, 133; 207, 403, 558 and 725 days was  
determined. In essence, complementary RNA derived from mice  
30       of different ages was screened for hybridization with  
oligonucleotide probes each specific to a particular mouse  
gene, each gene in turn representative of a particular mouse  
gene cluster (Unigene). Mouse genes which were  
differentially expressed (younger vs. older), as measured by  
35       different levels of hybridization of the respective cRNA  
samples with the particular probe corresponding to that  
mouse gene, were identified. Related human genes and  
proteins were identified by sequence comparisons to the



mouse gene or protein. In the international appl.  
Kopchick7A-PCT, filed June 2, 2004, we added some additional  
studies of CIDE-A (see below).

In a like manner, the effect of aging on the expression  
of genes in mouse skeletal muscle was studied, see  
provisional application Ser. No. 60/566,068, filed April 29,  
2004 (our docket Kopchick14-USA).

*Anti-Diabetes Applications.* In U.S. Provisional Appl.  
Ser. No. 60/458,398 (our docket Kelder1-USA), filed March  
31, 2003, members of our research group describe the  
identification of genes differentially expressed in normal  
vs. hyperinsulinemic, hyperinsulinemic vs. type II diabetic,  
or normal vs. type II diabetic mouse **liver**. Forward- and  
reverse-subtracted cDNA libraries were prepared, clones  
were isolated, and differentially expressed cDNA inserts  
were sequenced and compared with sequences in publicly  
available sequence databases. The corresponding mouse and  
human genes and proteins were identified.

The purpose of our research group's provisional  
application Ser. No. 60/460,415 (our docket: Kopchick6-  
USA), filed April 7, 2003, was similar, but complementary  
RNA, derived from RNA of mouse **liver**, was screened against a  
mouse gene chip. See also 60/506,716, filed Sept. 30, 2003  
(Kopchick6.1).

Gene chip analyses have also been used to identify  
genes differentially expressed in normal vs.  
hyperinsulinemic, hyperinsulinemic vs. type II diabetic, or  
normal vs. type II diabetic mouse **pancreas**, see U.S.  
Provisional Appl. 60/517,376, filed Nov. 6, 2003  
(Kopchick12) and **muscle**, see U.S. Provisional Appl.  
60/547,512, filed Feb. 26, 2004 (Kopchick15).

*Other differential hybridization applications.* The use  
of differential hybridization to identify genes and proteins  
is also described in our research group's Ser. No.  
PCT/US00/12145 (Kopchick 3A-PCT), Ser. No. PCT/US00/12366  
(Kopchick4A-PCT), and Ser. No. 60/400,052 (Kopchick5).

All of the foregoing applications are hereby incorporated by reference in their entirety.

5     **BACKGROUND OF THE INVENTION**

Field of the Invention

          The invention relates to various nucleic acid molecules and proteins, and their use in (1) diagnosing hyperinsulinemia and type II diabetes, or conditions  
10    associated with their development, and (2) protecting mammals (including humans) against them.

Description of the Background Art

15

**Diabetes**

          A deficiency of insulin in the body results in diabetes mellitus, which affects about 18 million individuals in the United States. It is characterized by a high blood glucose  
20    (sugar) level and glucose spilling into the urine due to a deficiency of insulin. As more glucose concentrates in the urine, more water is excreted, resulting in extreme thirst, rapid weight loss, drowsiness, fatigue, and possibly dehydration. Because the cells of the diabetic cannot use  
25    glucose for fuel, the body uses stored protein and fat for energy, which leads to a buildup of acid (acidosis) in the blood. If this condition is prolonged, the person can fall into a diabetic coma, characterized by deep labored breathing and fruity-odored breath.

30        There are two types of diabetes mellitus, Type I and Type II. Type II diabetes is the predominant form found in the Western world; fewer than 8% of diabetic Americans have the type I disease.

35        *Type I diabetes.* In Type I diabetes, formerly called juvenile-onset or insulin-dependent diabetes mellitus, the pancreas cannot produce insulin. People with Type I diabetes must have daily insulin injections. But they need to avoid taking too much insulin because that can lead to insulin

shock, which begins with a mild hunger. This is quickly followed by sweating, shallow breathing, dizziness, palpitations, trembling, and mental confusion. As the blood sugar falls, the body tries to compensate by breaking down fat and protein to make more sugar. Eventually, low blood sugar leads to a decrease in the sugar supply to the brain, resulting in a loss of consciousness. Eating a sugary food can prevent insulin shock until appropriate medical measures can be taken.

Type I diabetics are often characterized by their low or absent levels of circulating endogenous insulin, i.e., hypoinsulinemia (1). Islet cell antibodies causing damage to the pancreas are frequently present at diagnosis. Injection of exogenous insulin is required to prevent ketosis and sustain life.

*Type II diabetes.* Type II diabetes, formerly called adult-onset or non-insulin-dependent diabetes mellitus (NIDDM), can occur at any age. The pancreas can produce insulin, but the cells do not respond to it.

Type II diabetes is a metabolic disorder that affects approximately 17 million Americans. It is estimated that another 10 million individuals are "prone" to becoming diabetic. These vulnerable individuals can become resistant to insulin, a pancreatic hormone that signals glucose (blood sugar) uptake by fat and muscle. In order to maintain normal glucose levels, the islet cells of the pancreas produce more insulin, resulting in a condition called hyperinsulinemia. When the pancreas can no longer produce enough insulin to compensate for the insulin resistance, and thereby maintain normal glucose levels, hyperglycemia (elevated blood glucose) results, and type II diabetes is diagnosed.

Early Type II diabetics are often characterized by hyperinsulinemia and resistance to insulin. Late Type II diabetics may be normoinsulinemic or hypoinsulinemic. Type II diabetics are usually not insulin dependent or prone to ketosis under normal circumstances.

Little is known about the disease progression from the

normoinsulinemic state to the hyperinsulinemic state, and from the hyperinsulinemic state to the Type II diabetic state.

As stated above, type II diabetes is a metabolic disorder that is characterized by insulin resistance and impaired glucose-stimulated insulin secretion (2,3,4). However, Type II diabetes and atherosclerotic disease are viewed as consequences of having the insulin resistance syndrome (IRS) for many years (5). The current theory of the pathogenesis of Type II diabetes is often referred to as the "insulin resistance/islet cell exhaustion" theory. According to this theory, a condition causing insulin resistance compels the pancreatic islet cells to hypersecrete insulin in order to maintain glucose homeostasis. However, after many years of hypersecretion, the islet cells eventually fail and the symptoms of clinical diabetes are manifested. Therefore, this theory implies that, at some point, peripheral hyperinsulinemia will be an antecedent of Type II diabetes. Peripheral hyperinsulinemia can be viewed as the difference between what is produced by the  $\beta$  cell minus that which is taken up by the liver. Therefore, peripheral hyperinsulinemia can be caused by increased  $\beta$  cell production, decreased hepatic uptake or some combination of both. It is also important to note that it is not possible to determine the origin of insulin resistance once it is established since the onset of peripheral hyperinsulinemia leads to a condition of global insulin resistance.

Multiple environmental and genetic factors are involved in the development of insulin resistance, hyperinsulinemia and type II diabetes. An important risk factor for the development of insulin resistance, hyperinsulinemia and type II diabetes is obesity, particularly visceral obesity (6,7,8). Type II diabetes exists world-wide, but in developed societies, the prevalence has risen as the average age of the population increases and the average individual becomes more obese.

*Obesity and Diabetes.* Obesity is a serious and growing

problem in the United States. Obesity-related health risks include high blood pressure, hardening of the arteries, cardiovascular disease, and Type II diabetes (also known as non-insulin-dependent diabetes mellitus, Type II diabetes) (9,10,11). Recent studies show that 85% of the individuals with Type II diabetes are obese (12).

*Treatment of Diabetes.* For many years, treatment was insulin therapy for Type I and oral sulfonylureas and/or insulin therapy for Type II. Metformin (glucophage) was the first antidiabetic drug approved by FDA (May 1995) for the treatment of Type II diabetes since the oral sulfonylureas were introduced in 1984. Metformin promotes the use of insulin already in the blood. This May 1995 approval was followed by the September 1995 approval of another antidiabetic drug, Acarbose (precose). It slows down the digestion and absorption of complex sugars, which reduces blood sugar levels after meals.

Before 1982, insulin was purified from beef or pork pancreas. This was a problem for those diabetics allergic to animal insulin. Researchers produced a synthetic insulin called humulin. Approved by FDA in 1982, it was the first genetically engineered consumer health product manufactured for diabetics. Synthetic insulins can be produced in unlimited quantities.

Another possible treatment for diabetes includes surgically replacing the pancreas' endocrine tissues (islets of Langerhans) with healthy islet of Langerhans tissue grafts. Since 1988, 45 patients worldwide have undergone successful transplantation.

*Complications.* Complications of diabetes (end organ damage) include retinopathy, neuropathy, and nephropathy (traditionally designated as microvascular complications) as well as atherosclerosis (a macrovascular complication). Early stages of hyperglycemia can usually be controlled by an alteration in diet and increasing the amount of exercise, but drug treatment, including insulin, may be required. It has been shown that meticulous blood glucose control can

often slow down or halt the progression of diabetic complications if caught early enough (1). However, tight metabolic control is extremely difficult to achieve.

5

### **Animal Models**

*Transgenic Mouse Models of Diabetes or Diabetes Resistance.* McGrane, et al., J. Biol. Chem. 263:11443-51 (1988) and Chen, et al., J. Biol. Chem., 269:15892-7 (1994) describe the genetic engineering of mice to express bovine growth hormone (bGH) or human growth hormone (hGH), respectively. These mice exhibited an enhanced growth phenotype. They also developed kidney lesions similar to those seen in diabetic glomerulosclerosis, see Yang, et al., Lab. Invest., 68:62-70 (1993). Ogueta, et al., J. Endocrinol., 165: 321-8 (2000) reported that transgenic mice expressing bovine GH develop arthritic disorder and self-antibodies.

Growth hormone has many roles, ranging from regulation of protein, fat and carbohydrate metabolism to growth promotion. GH is produced in the somatrophic cells of the anterior pituitary and exerts its effects either through the GH-induced action of IGF-I, in the case of growth promotion, or by direct interaction with the GHR on target cells including liver, muscle, adipose, and kidney cells. Hyposecretion of GH during development leads to dwarfism, and hypersecretion before puberty leads to gigantism. In adults, hypersecretion of GH results in acromegaly, a clinical condition characterized by enlarged facial bones, hands, feet, fatigue and an increase in weight. Of those individuals with acromegaly, 25% develop type II diabetes. This may be due to insulin resistance caused by the high circulating levels of GH leading to high circulating levels of insulin (Kopchick et al., Annual Rev. Nutrition 1999. 19:437-61).

A further mode of GH action may be through the transcriptional regulation of a number of genes contributing to the physiological effects of GH.

Growth hormone genes and the proteins encoded by them can be converted into growth hormone antagonists by mutation, see Kopchick USP 5,350,836. Transgenic mice have been made that express the GH antagonists bGH-G119R or hGH G120R, and which exhibit a dwarf phenotype. Chen, et al., J. Biol. Chem., 263:15892-7 (1994); Chen, et al., Mol. Endocrinol, 5:1845-52 (1991); Chen, et al., Proc. Nat. Acad. Sci. USA 87:5061-5 (1990). These mice did not develop kidney lesions. See Yang (1993), supra.

Chen, et al., Endocrinol, 136:660-7 (1995) compared the effect of streptozotocin treatment in normal nontransgenic mice, and in mice transgenic for (1) a GH receptor antagonist, the G119R mutant of bovine growth hormone or (2) the E117L-mutant of bGH. (According to Chen's ref. 24, these large GH transgenic streptozotocin-treated mice constitute an animal model for diabetes.) Glomerulosclerosis was seen in diabetic (STZ-treated) nontransgenic mice and in diabetic bGH-E117L mice, but not in diabetic bGH-G119R (GH antagonist) mice.

Two of the proteins which mediate growth hormone activity are the growth hormone receptor and the growth hormone binding protein, encoded by the same gene in mice (GHR/BP). It is possible to genetically engineer mice so that the gene encoding these proteins is disrupted ("knocked-out"; inactivated), see Zhou, et al., Proc. Nat. Acad. Sci. (USA), 94:13215-20 (1997). Zhou, et al. inactivated the GHR/BP gene by replacing the 3' portion of exon 4 (which encodes a portion of the GH binding domains) and the 5' region of intron 4 with a neomycin gene cassette. The modified gene was introduced into the target mice by homologous recombination. Like mice expressing a GH antagonist, homozygous GHR/BP-KO mice exhibit a dwarf phenotype. GHR/BP-KO mice, made diabetic by streptozotocin treatment, are protected from the development of diabetes-associated nephropathy. Bellush, et al., Endocrinol., 141:163-8 (2000).

*High-Fat Diets.* High-fat diets have been shown to induce both obesity and Type II diabetes in laboratory

animals (13). Surwit and colleagues demonstrated that male C57BL/6J mice are extremely sensitive to the diabetogenic effects of a high-fat diet when initiated at weaning. At six months of age, high-fat fed animals had significantly elevated fasting blood-glucose and insulin levels and also demonstrated a decrease in insulin sensitivity (14). Ahren and colleagues (15) reported evidence of insulin resistance as well as diminished glucose-stimulated insulin release, after feeding with a high-fat diet for 12 weeks. These mice also showed elevated levels of total cholesterol, triglycerides, and free fatty acids, another hallmark of Type II diabetes.

#### 15 **Anatomy and Physiology of Muscle**

Muscle tissue constitutes about 40% of the body mass. Muscles may be classified by location, i.e., skeletal if attached to bone, cardiac if forming the wall of the heart, and visceral if associated with another body organ. Muscles may also be classified as voluntary or involuntary, depending on how their contractions and relaxations are controlled. Skeletal muscles are voluntary, while cardiac and visceral muscles are involuntary. It is also possible to classify muscles morphologically; skeletal and cardiac muscle cells are striated, whereas visceral muscle cells are not.

Each skeletal muscle is composed of many individual muscle cells called muscle fibers. The fibers are held together by fibrous connective-tissue membranes called fascia. The fascium which envelops the entire muscle is the epimysium, and the fascia which penetrate the muscle, separating the fibers into bundles (fasciculi) are called perimysium. Very thin fascia (endomysium) sheath each muscle fiber. Skeletal muscles are attached either directly to a bone, or indirectly through a tendon.

The individual muscle fibers (cells) comprise threadlike protein structures called myofibrils.



There are over 600 muscles in the human body. We will have occasion later to refer to the gastrocnemius. It is a superficial muscle in the posterior compartment of the lower leg, which together with the underlying soleus forms the characteristic bulge of the calf.

### **Role of Muscle in Development of Type II Diabetes**

Muscle, fat and liver tissues are the major contributors to the development of insulin resistance, hyperinsulinemia, and, ultimately, type II diabetes. Muscle cells respond to insulin by increasing glucose uptake from the bloodstream. Muscle tissue can become resistant to insulin, causing the beta cells to initially increase insulin secretion. Eventually, though, the beta cells become unable to compensate for this increasing insulin resistance from muscle and other cells, and they fail to respond to elevated blood glucose levels. Thus, clinical type 2 diabetes results from the combination of insulin resistance and impaired beta cell function.

Defects in muscle glycogen synthesis are known to play a role in the development of insulin resistance. At least three steps—those mediated by glycogen synthase, hexokinase, and GLUT4—have been reported to be defective in patients with type 2 diabetes.

Fatty acids can induce insulin resistance, and it has been suggested that this was a consequence of altered insulin signaling through PI3-kinase. PKC- $\theta$  has also been implicated.

See generally Petersen, et al., "Pathogenesis of Skeletal muscle insulin resistance in type 2 diabetes mellitus", in "A Symposium: Evolution of type 2 diabetes mellitus management", at *Amer. J. Cardiol.*, 90(5A): 11G-18G, (Sept. 5, 2002).

### **Adverse Effects of Type II Diabetes on Muscle**

"Myopathy is a general term used to describe any disease of muscles, such as the muscular dystrophies and myopathies associated with thyroid disease. It can be caused

by endocrine disorders, including diabetes, metabolic disorders, infection or inflammation of the muscle, certain drugs and mutations in genes. In diabetes, myopathy is thought to be caused by neuropathy, a complication of diabetes. General symptoms of myopathies include muscle weakness of limbs sometimes occurring during exercise although in some cases the symptoms diminish as exercise increases. Depending on the type of myopathy, one muscle group may be more affected than others." See "Joint and Muscle Problems Associated with Diabetes", [www.iddtinternational.org/jointandmuscleproblems.html](http://www.iddtinternational.org/jointandmuscleproblems.html) [Last modified June 12, 2003].

Diabetic muscle infarction can spontaneously affect patients with a long history of poorly controlled diabetes. "Most affected patients have multiple microvascular complications (neuropathy, nephropathy, and retinopathy). The clinical presentation is an acute onset of pain and swelling over days to weeks in the affected muscle groups (usually the thigh or calf), along with varying degrees of tenderness.... Therapy consists of rest and analgesia. Routine daily activities are not deleterious to the condition, but physical therapy may cause exacerbation. Spontaneous diabetic muscle infarction tends to resolve over a period of weeks to months in most cases." See "Musculoskeletal Complications of Diabetes - Part 2", [www.diabetic-lifestyle.com/articles/jan02\\_whats\\_1.htm](http://www.diabetic-lifestyle.com/articles/jan02_whats_1.htm) [last modified Feb. 9, 2004]. See also Trujillo-Santos, et al., "Diabetes muscle infarction: an underdiagnosed complication of long-standing diabetes," Diabetes Care, 26(1):211-5 (2003).

### **Identification of genes involved in hyperinsulinemia and type II diabetes, generally**

5        Our attention recently has focused on the generation of muscle mRNA expression profiles and the identification of genes involved in the genesis of the obesity-induced hyperinsulinemia and type-II diabetes. To date, no one has attempted to study the actual progression from the normal  
10       condition to that of hyperinsulinemia or from hyperinsulinemia to Type II diabetes in an attempt to identify genes that are up-regulated or down-regulated in muscle as the disease progresses.

15       In previous studies aimed at identifying genes involved in diabetes-induced glomerulosclerosis, differential display and traditional subtractive hybridization techniques were used (16-20). While effective for the identification of a few genes (e.g. hmunc13, PED/PEA-15, lactate dehydrogenase, amiloride sensitive sodium channel, ubiquitin-like protein,  
20       mdrl, and  $\alpha$ -amyloid protein precursor as well as a few novel genes), these techniques can be quite labor intensive. The PCR-based method of subtractive hybridization requires less starting material, and allows the simultaneous isolation of all differentially expressed cDNAs into two  
25       groups (up-regulated and down-regulated).

30       However, the PCR-based method of subtractive hybridization is also quite labor-intensive, produced large numbers of false positive candidates and ultimately resulted in the identification of a relatively limited number of differentially expressed genes. (see Kelder1-USA application).

35       In order to expand the number of genes that can be analyzed simultaneously, several groups have begun to utilize DNA microarray analysis to measure differences in gene expression between normal and diseased states. However, these experiments have been limited in regards to the number of experimental conditions analyzed. DNA microarray analysis has been performed on normal, obese and diabetic mice (21). Also, the obesity and diabetes in the

mouse models examined were caused by a specific endogenous genetic mutation (22). The differentially expressed genes in the above models may be very different from genes differentially expressed due to diet-induced obesity and Type-II diabetes.

The use of differential expression and related techniques to identify genes useful in the treatment of diabetes has been reviewed by Perfetti, et al., *Diabetes Technol. & Therapeut.*, 5(3): 421-3 (2003). Bernal-Mizrachi, et al., *Diabetes Metab. Res. Rev.* 19: 32-42 (2003).

Other papers of interest include:

Wada, et al., "Gene expression profile in streptozotocin-induced diabetic mice kidneys undergoing glomerulosclerosis", *Kidney Int.*, 59:1363-73 (2001);

Song, et al., "Cloning of a novel gene in the human kidney homologous to rat munc13S: its potential role in diabetic nephropathy", *Kidney Int.*, 53:1689-95 (1998);

Page, et al., "Isolation of diabetes-associated kidney genes using differential display", *Biochem. Biophys. Res. Comm.*, 232:49-53 (1997).

Peradi, "Subtractive hybridization claims: An efficient technique to detect overexpressed mRNAs in diabetic nephropathy," *Kidney Int.* 53:926-31 (1998).

Condorelli, *EMBO J.*, 17:3858-66 (1998).

#### **Diabetes-Specific Differential Expression in Muscle**

Sreekumar, et al., "Gene expression profile in skeletal muscle of type 2 diabetes and the effect of insulin treatment," *Diabetes* 51: 1913 (June 2002) surveyed 6,451 genes, and identified 85 genes for which there was an alteration in skeletal muscle transcription in diabetic patients after withdrawal of insulin treatment. Subsequent insulin treatment resulted in further changes in transcription of 74 of the 85 genes (15 increased, 59 decreased), and also resulted in alteration of 29 additional gene transcripts.

Mootha, et al., "PCG-1 $\alpha$  responsive genes involved in oxidative phosphorylation are coordinatively downregulated in human diabetes," *Nature Genetics* 34(3); 267 (July 2003),  
5 used DNA microarrays to detect changes in the expression of sets of related genes, rather than of individual genes. They classified over 22,000 genes into 149 data sets; some of these data sets overlapped. They looked for a statistical correlation between the overall rank order of the genes in  
10 differential expression, and the groups to which the genes belonged. Expression was compared pairwise among three groups: males with normal glucose tolerance; males with impaired glucose tolerance; and males with type 2 diabetes. The set with the highest enrichment score (the one whose  
15 members ranked highly most often relative to chance expectation) was an internally curated set of 106 genes involved in oxidative phosphorylation. While the average decrease for the individual genes was modest (~20%), it was also consistent, being observed in 89% (94/106) of the genes  
20 in question. This paper is reviewed by Toye and Gauguier, "Genetics and functional genomics of type 2 diabetes mellitus", *Genome Biology*, 4: 241 (2003).

Patti, et al., "Coordinated reduction of genes of oxidative  
25 metabolism in humans with insulin resistance and diabetes: Potential role of PGC1 and NRF1", *Proc. Nat. Acad. Sci. (USA)*, 100(14): 8466 (July 8, 2003) used microarrays to analyze skeletal muscle expression of genes in nondiabetic insulin-resistant subjects at high risk for diabetes (based  
30 on family history of diabetes and Mexican-American ethnicity) and diabetic Mexican-American subjects. Of 7,129 sequences represented on the microarray, 187 were differentially expressed between control and diabetic subjects. However, no single gene remained significantly  
35 differentially expressed after controlling for multiple comparison false discovery by using the Benjamini-Hochberg method, see Benjamini, et al., *J. R. Stat. Soc. Ser. B.* 57:289-300 (1995); Dudait, et al., *Stat. Sin.* 12: 111-139 (2002). Consequently, Patti et al. sought to identify

groups of related genes with similar patterns of differential expression using MAPP FINDER and ONTOEXPRESS. According to MAPP FINDER, the top-ranked cellular component terms were mitochondrion, mitochondrial membrane, mitochondrial inner membrane, and ribosome, and the top-ranked process term was ATP biosynthesis. According to ONTOEXPRESS, the over-represented groups were energy generation, protein biosynthesis/ribosomal proteins, RNA binding, ribosomal structural protein, and ATP synthase complex.

Huang, Xudong, "Identification of abnormally expressed genes in skeletal muscle contributing to insulin resistance and type 2 diabetes", Thesis, document id: 9576 Lunds University 2002, reported differential expression of the mitochondrially-encoded ND1 gene in human diabetic patients and of the nuclear-encoded cathepsin L gene in mice.

Standaert, et al., "Skeletal muscle insulin resistance in obesity-associated type 2 diabetes in monkeys is linked to a defect in insulin activation of protein kinase C-zeta/lambda/iota Diabetes 51: 2936 (Oct. 2002). the authors concluded that defective activation of atypical PKCs played an important role in the pathogenesis of peripheral insulin resistance in both obese prediabetic and diabetic monkeys. They attributed this linkage to the apparent requirement for aPKCs during insulin-stimulated glucose transport.

Srommer, et al., Am. J. Physiol., "Skeletal muscle insulin resistance after trauma: insulin signaling and glucose transport", 275(2 Pt. 1): E3518(Aug. 1998) concluded that insulin resistance in skeletal muscle after surgical trauma is associated with reduced glucose transport but not with impaired glucose signaling to PI 3-kinase or its downstream target, Akt.

#### **Aging-Specific Differential Expression in Muscle**

***Gene Chip-Based Identification of genes involved in aging of skeletal muscle***

Several groups have used DNA microarrays to measure differences in gene expression caused by the aging process. However, these experiments are extremely limited in regards to the number of aging time points or experimental conditions.

Weindruch, et al., "Microarray profiling of gene expression in aging and its alteration by caloric restriction in mice" in Symposium: Calorie Restriction: effects on Body Composition, Insulin Signaling and Aging 918S-923S (2001) (21) compared expression in gastrocnemius muscle from 5- and 30-month old C57BL/6 mice, with and without caloric restriction. In this analysis, the expression of 113 genes was found to be changed by at least two-fold in 5-month old mice compared to 30-month old mice. Caloric restriction of comparable mice caused a reversal of the altered gene expression of 33 genes.

Of the 6347 genes surveyed in the oligonucleotide microarray, only 58 (0.9%) displayed a greater than 2 fold increase in gene expression as a function of aging, whereas 55(0.9%) displayed a greater than 2 fold decrease.

Of the genes positively correlated with aging, 16% could be assigned to stress responses. The largest differential expression between young and aged animals (3.8 fold) was the mitochondrial sarcomeric creatine kinase.

Of the genes negatively correlated with aging, 13% were involved in energy metabolism. A noteworthy number were genes encoding biosynthetic enzymes (cytochrome P450 IIC12, squaelene synthase, stearoyl-CoA desaturase, EF-1-gamma. Another down regulator was a CpG binding protein, MeCP2.

Weindruch further reported that age-related changes in gene expression profile were "remarkably attenuated" by caloric restriction.

What appears to be the same experiment is discussed in Lee, et al., "Gene expression profile of aging and its retardation by caloric restriction," Science, 285: 1390 (Aug. 27, 1999). This papers lists the individual genes which

were differentially expressed by more than 2-fold, and classifies them as energy metabolism, neuronal factors, protein metabolism, stress response, biosynthesis, calcium metabolism or DNA repair genes.

Welle, et al., "Skeletal muscle gene expression profiles in 20-29 year old and 65-71 year old women," *Exper. Gerontol.*, 39: 369-77 (2004) and available electronically as doi:10.1016/j.exger.2003.11.011 studied gene expression and physical condition in seven young and eight older women.

With respect to physical condition, the measured or calculated parameters were total body mass, lean body mass, left leg lean mass (by biopsy), maximum isometric left knee extension force, left knee extension force/left leg lean mass, Peak  $\text{VO}_2$ /lean body mass, and Peak  $\text{VO}_2$ /left leg lean mass.

There were 1178 "probe sets" (representing 1053 different Unigene clusters) for which differential expression was detected; 550 for which expression was higher in older women, and 628 the inverse effect. The differences ranged from 1.2 to 4 fold; most (78A%) were less than 1.5 fold. The complete list of differentially expressed genes is given in the Rochester Muscle database website, [www.urmc.rochester.edu/smd/crc/swindex](http://www.urmc.rochester.edu/smd/crc/swindex) (".html" omitted, in accordance with USPTO requirements, so that the publication of this application will not create an active hyperlink).

The gene most highly overexpressed in older muscle was p21 (cyclin-dependent kinase inhibitor 1A) (4.01 fold). This one of several genes (see Welle Table 2) which are potentially related to DNA damage and repair. Welle also thought it noteworthy how many of the differentially expressed genes were ones that encode proteins which bind to pre-mRNAs or mRNAs (see Welle Table 3).

#### ***Other Differential/Subtractive Hybridization Studies of Interest***

Zhang, et al., *Kidney International*, 56:549-558 (1999) identified genes up-regulated in 5/6 nephrectomized



(subtotal renal ablation) mouse kidney by a PCR-based subtraction method. Ten known and nine novel genes were identified. The ultimate goal was to identify genes involved in glomerular hyperfiltration and hypertrophy. Melia, et al., *Endocrinol.*, 139:688-95 (1998) applied subtractive hybridization methods for the identification of androgen-regulated genes in mouse kidney. The treatment mice were dosed with dihydrotestosterone, an androgen. Kidney androgen-regulated protein gene was used as a positive control, as it is known to be up-regulated by DHT.

See also Holland, et al., Abstract 607, "Identification of Genes Possibly Involved in Nephropathy of Bovine Growth Hormone Transgenic Mice" (Endocrine Society Meeting, June 22, 2000) and Coschigano, et al., Abstract 333, "Identification of Genes Potentially Involved in Kidney Protection During Diabetes" (Endocrine Society Meeting, June 22, 2000).

The following differential hybridization articles may also be of interest: Wada, et al., "Gene expression profile in streptozotocin-induced diabetic mice kidneys undergoing glomerulosclerosis", *Kidney Int.*, 59:1363-73 (2001); Song, et al., "Cloning of a novel gene in the human kidney homologous to rat munc13S: its potential role in diabetic nephropathy", *Kidney Int.*, 53:1689-95 (1998); Page, et al., "Isolation of diabetes-associated kidney genes using differential display", *Biochem. Biophys. Res. Comm.*, 232:49-53 (1997); Peradi, "Subtractive hybridization claims: An efficient technique to detect overexpressed mRNAs in diabetic nephropathy," *Kidney Int.* 53:926-31 (1998); Condorelli, *EMBO J.*, 17:3858-66 (1998).

### **Apoptosis and *CIDE-A***

Apoptosis is a form of programmed cell death that occurs in an active and controlled manner to eliminate unwanted cells. Apoptotic cells undergo an orchestrated cascade of morphological changes such as membrane blebbing,

nuclear shrinkage, chromatin condensation, and formation of apoptotic bodies which then undergo phagocytosis by neighboring cells. One of the hallmarks of cellular apoptosis is the cleavage of chromosomal DNA into discrete oligonucleosomal size fragments. This orderly removal of unwanted cells minimizes the release of cellular components that may affect neighboring tissue. In contrast, membrane rupture and release of cellular components during necrosis often leads to tissue inflammation.

The process of apoptosis is highly conserved and involves the activation of the caspase cascade. Cohen, GM. (1997) Caspases: the executioners of apoptosis. *Biochem. J.* 326:1-16; Budihardjo, I., Oliver, H., Lutter, M., Luo, X., Wang, X. (1999) Biochemical pathways of caspase activation during apoptosis. *Annu. Rev. Cell. Dev. Biol.* 15:269-290; Jacobson, M.D., Weil, M., Raff, M.C. (1997) Programmed cell death in animal development. *Cell* 88:347-354. Caspases are a family of serine proteases that are synthesized as inactive proenzymes. Their activation by apoptotic signals such as CD95 (Fas) death receptor activation or tumor necrosis factor results in the cleavage of specific target proteins and execution of the apoptotic program. Apoptosis may occur by either an extrinsic pathway involving the activation of cell surface death receptors (DR) or by an intrinsic mitochondrial pathway. Yoon, J-H. Gores G.J. (2002) Death receptor-mediated apoptosis and the liver. *J. Hepatology* 37:400-410.

These pathways are not mutually exclusive and some cell types require the activation of both pathways for maximal apoptotic signaling. In type-I cells, death receptor activation leads to the recruitment and activation of caspases-8/10 and the rapid cleavage and activation of caspase-3 in a mitochondrial-independent manner.

Hepatocytes are members of the Type-II cells in which mitochondria are essential for DR-mediated apoptosis Scaffidi, C., Fulda, S., Srinivasan, A., Friesen, C., Li, F., Tomaselli, K.J., Debatin, K.M., Krammer, P.H., Peter, M.E. (1998) Two CD95 (APO-1/Fas) signaling pathways. *EMBO J.* 17:1675-1687. In this pathway, the pro-apoptotic protein

Bid is truncated by activated caspases-8/10 and translocates to the mitochondria. Luo, X., Budihardjo, I., Zou, H., Slaughter, C., Wang, X. (1998) Bid, a Bcl2 interacting protein, mediates cytochrome c release from mitochondria in response to activation of cell surface death receptors. *Cell* 94:481-490; Li, H., Zhu, H., Xu, C.J., Yuan, J. (1998) Cleavage of BID by caspase 8 mediates the mitochondrial damage in the Fas pathway of apoptosis. *Cell* 94:491-501. This translocation leads to mitochondrial cytochrome c release and eventual activation of caspases-3 and 7 via cleavage by activated caspase-9.

One of the substrates for activated caspase-3 is the DNA fragmentation factor (DFF). DFF is composed of a 45 kDa regulatory subunit (DFF45) and a 40 kDa catalytic subunit (DFF40). Liu, X., Zou, H., Slaughter, C., Wang, X. (1997) DFF, a heterodimeric protein that functions downstream of caspase-3 to trigger DNA fragmentation during apoptosis. *Cell* 89:175-184. DFF45 cleavage by activated caspase-3 results in its dissociation from DFF40 and allows the caspase-activated DNase (CAD) activity of DFF40 to cleave chromosomal DNA into oligonucleosomal size fragments. Liu, X., Li, P., Widlak, P., Zou, H., Luo, X., Garrard, W.T., Wang, X. (1998) The 40-kDa subunit of DNA fragmentation factor induces DNA fragmentation and chromatin condensation during apoptosis. *Proc. Natl. Acad. Sci. USA*. 95:8461-8466; Halenbeck, R., MacDonald, H., Roulston, A., Chen, T.T., Conroy, L., Williams, L.T. (1998) CPAN, a human nuclease regulated by the caspase-sensitive inhibitor DFF45. *Curr Biol*. 8:537-540; Nagata, S. (2000) Apoptotic DNA fragmentation. *Exp. Cell Res.* 256:12-8.

Recently, a novel family of cell-death-inducing DFF45-like effectors (CIDEs) have been identified that includes CIDE-A, CIDE-B and CIDE-3/FSP2. Inohara, N., Koseki, T., Chen, S., Wu, X., Nunez, G. (1998) CIDE, a novel family of cell death activators with homology to the 45 kDa subunit of the DNA fragmentation factor. *EMBO J.* 17:2526-2533; Danesch, U., Hoeck, W., Ringold, G.M. (1992) Cloning and transcriptional regulation of a novel adipocyte-specific gene, FSP27. CAAT-enhancer-binding protein (C/EBP)

and C/EBP-like proteins interact with sequences required for differentiation-dependent expression. *J. Biol. Chem.* 267:7185-7193; Liang, L., Zhao, M., Xu, Z., Yokoyama, K.K., Li, T. (2003) Molecular cloning and characterization of CIDE-3, a novel member of the cell-death-inducing DNA-fragmentation-factor (DFF45)-like effector family. *Biochem. J.* 370:195-203.

The CIDEs contain an N-terminal domain that shares homology with the N-terminal region of DFF45 and may represent a regulatory region via protein interaction. See Inohara, supra; Lugovskoy, A.A., Zhou, P., Chou, J.J., McCarty, J.S., Li, P., Wagner, G. (1999) Solution structure of the CIDE-N domain of CIDE-B and a model for CIDE-N/CIDE-N interactions in the DNA fragmentation pathway of apoptosis. *Cell* 9:747-755. The family members also share a C-terminal domain that is necessary and sufficient for inducing cell death and DNA fragmentation; see Inohara supra. The overexpression of CIDE-A induces cell death that can be inhibited by DFF45. However, CIDE-A-induced apoptosis is not inhibited by caspase-8 inhibitors thereby suggesting the presence of additional, caspase-independent, pathway(s) for the induction of apoptosis, see Inohara supra. Previous reports have indicated that human and mouse CIDE-A are expressed in several tissues such as brown adipose tissue (BAT) and heart and are localized to the mitochondria, Zhou, Z., Yon Toh, S., Chen, Z., Guo, K., Ng, C.P., Ponniah, S., Lin, S.C., Hong, W., Li, P. (2003) Cidea-deficient mice have lean phenotype and are resistant to obesity. *Nat. Genet.* 35:49-56. . In addition to the ability to induce apoptosis, CIDE-A can interact and inhibit UCP1 in BAT and may therefore play a role in regulating energy balance, see Zhou supra.

Previous reports have indicated that CIDE-A is not expressed in either adult human or mouse liver tissue, see Inohara supra, Zhou supra.

The human protein cell death activator CIDE-A is of particular interest because of its highly dramatic change in liver expression with age, first demonstrated in our

Kopchick7 application, supra. CIDE-A expression is elevated in older normal mice. CIDE-A expression was studied for normal C57BI/6J mouse ages 35, 49, 77, 133, 207, 403 and 558 days. Expression is low at the first five data points, then rises sharply at 403 days, and again at 558 days.

CIDE-A was therefore classified as an "unfavorable protein", i.e., it was taught that an antagonist to CIDE-A could retard biological aging.

In Kopchick7A-PCT we reported that CIDE-A is also prematurely expressed in hyperinsulinemic and type-II diabetic mouse liver tissue. CIDE-A expression also correlates with liver steatosis in diet-induced obesity, hyperinsulinemia and type-II diabetes. These observations suggest an additional pathway of apoptotic cell death in Non-Alcoholic Fatty Liver Disease (NAFLD) and that CIDE-A may play a role in this serious disease and potentially in liver dysfunction associated with type-II diabetes.

**SUMMARY OF THE INVENTION**

Differential hybridization techniques have been used to identify mouse genes that are differentially expressed in the **muscle** (gastrocnemius) of mice, depending upon their development of hyperinsulinemia or type II diabetes.

In essence, complementary RNA derived from normal mice, or mouse models of hyperinsulinemia or type II diabetes, was screened for hybridization with oligonucleotide probes each specific to a particular mouse database DNA, the latter being identified, by database accession number, by the gene manufacturer. Each database DNA in turn was also identified by the gene chip manufacturer as representative of a particular mouse gene cluster (Unigene).

In most cases, this database DNA sequence is a full length genomic DNA or cDNA sequence, and is therefore either identical to, or otherwise encodes the same protein as does, a natural full-length genomic DNA protein coding sequence. Those which don't present at least a partial sequence of a natural gene or its cDNA equivalent.

For the sake of simplicity, all of these mouse database DNA sequences, whether full-length or partial, and whether cDNA or genomic DNA, are referred to herein as "mouse genes". When only the genomic sequence is intended, we will refer specifically to "genomic DNA" or "gDNA".

The sequences in the protein databases are determined either by directly sequencing the protein or, more commonly, by sequencing a DNA, and then determining the translated amino acid sequence in accordance with the Genetic Code. All of the mouse sequences in the mouse polypeptide database are referred to herein as "mouse proteins" regardless of whether they are in fact full length sequences.

Mouse genes which were differentially expressed (normal vs. hyperinsulinemic, hyperinsulinemic vs. diabetic, or normal vs. diabetic), as measured by different levels of hybridization of the respective cRNA samples with the particular probe corresponding to that mouse gene) were identified.

Since the progression is from normal to hyperinsulinemic, and thence from hyperinsulinemic to type II diabetic, one may define mammalian subjects as being more favored or less favored, with normal subjects being more favored than hyperinsulinemic subjects, and hyperinsulinemic subjects being more favored than type II diabetic subjects. The subjects' state may then be correlated with their gene expression activity.

The terms "normal" and "control" are used interchangeably in this specification, unless expressly stated otherwise. The control or normal subject is a mouse which is normal vis-a-vis fasting insulin and fasting glucose levels. The term "normal", as used herein, means normal relative to those parameters, and does not necessitate that the mouse be normal in every respect.

A mouse gene is said to have exhibited a favorable behavior if, for a particular mouse age of observation, its average level of expression in mice which are in a more favored state is **higher** than that in mice which are in a less favored state. A mouse gene is said to have exhibited an unfavorable behavior if, for a particular mouse age of observation, its average level of expression in mice which are in a more favored state is **lower** than that in mice which are in a less favored state.

When we observe the mice at several different ages, it is possible for their expression behavior to vary from time point to time point. For a given comparison of subjects, e.g., normal vs. hyperinsulinemic, we classify the mouse gene as favorable or unfavorable on the basis of the direction of the largest expression change, and it is the magnitude of this largest expression change, expressed as a ratio of greater to lesser, which is set forth in the Master Table 1 data for that mouse gene. Thus, if at 2 weeks, there was a 3-fold favorable behavior, and at 8 weeks, there was a 4-fold unfavorable behavior, and at all other observed time points, the behavior was weaker than 3-fold, the mouse gene would be classified as an unfavorable gene with respect to the subject comparison in question.

It will be appreciated that it may be that if the mouse gene were observed at an age other than one of the ages noted in the Examples, we would have observed a still stronger differential expression behavior. Nonetheless, we must classify the mouse genes on the basis of the behavior which we actually observed, not the behavior which might have been observed at some other age.

We are particularly interested in mouse genes which exhibit strongly favorable or unfavorable differential expression behaviors. A behavior is considered strong if the ratio of the higher level to the lower level is at least two-fold.

However, a mouse gene may still be identified as favorable or unfavorable even if none of its observed behaviors are strong as defined above. In general, we consider the consistency of its behaviors (that is, are all or most of the differential expression behaviors at different ages in the same direction, e.g., hyperinsulinemic higher than control), the magnitude of the behaviors (higher the better), and the expression behavior of structurally or functionally related mouse genes (a mouse gene is more likely to be identified as favorable on the basis of a weakly favorable behavior if it is related to other mouse genes which exhibited favorable, especially strongly favorable, behavior). If we considered a mouse gene with only weak differential expression behavior to be worthy of consideration on the basis of these criteria, then we listed it in Master Table 1 in the appropriate subtable.

Preferably, the differential behavior observed is both strong and consistent. Preferably, if related mouse genes were tested, they exhibit the same direction of differential expression behavior.

A mouse gene which was more strongly expressed in hyperinsulinemic tissue than in either normal or type II diabetic tissue (i.e.,  $C < HI$ ,  $HI > D$ ) will be deemed both "unfavorable", by virtue of the control:hyperinsulinemic comparison, and "favorable", by virtue of the



hyperinsulinemic:diabetic comparison. This is one of several possible "mixed" expression patterns.

Thus, we can subdivide the "favorables" into wholly and partially favorables. Likewise, we can subdivide the  
5 unfavorables into wholly and partially unfavorables. The genes/proteins with "mixed" expression patterns are, by definition, both partially favorable and partially unfavorable. In general, use of the wholly favorable or wholly unfavorable genes/proteins is preferred to use of the  
10 partially favorable or partially unfavorable ones.

It is evident from the foregoing that mixed genes/proteins are those exhibiting a combination of favorable and unfavorable behavior. A mixed gene/protein can be used as would a favorable gene/protein if its  
15 favorable behavior outweighs the unfavorable. It can be used as would an unfavorable gene/protein if its unfavorable behavior outweighs the favorable. Preferably, they are used in conjunction with other agents that affect their balance of favorable and unfavorable behavior. Use of mixed  
20 genes/proteins is, in general, less desirable than use of purely favorable or purely unfavorable genes/proteins, but it is not excluded.

It should be noted that a mouse gene is classified on the basis of the strongest C-HI behavior among the ages  
25 tested, the strongest HI-D behavior among the ages tested, and the strongest C-D behavior among the ages tested. If at least one of these three behaviors is significantly favorable, and none of the others of these three behaviors is significantly unfavorable, the mouse gene will be  
30 classified as wholly favorable and listed in subtable 1A of Master Table 1. However, that does not mean that it may not have exhibited a weaker but unfavorable expression behavior at some tested age.

The "favorable", "unfavorable" and "mixed" mouse  
35 proteins of the present invention include the mouse database proteins listed in the Master Table in the same row as a particular "favorable", "unfavorable" or "mixed" mouse gene, respectively. These proteins may be the exact translation product of the identified mouse gene (database DNA).

However, if they were sequenced directly, they could be shorter or longer than that translation product. They could also differ in sequence from the exact translation product as a result of post-translational modifications.

5       The mouse proteins of interest also include mouse proteins which, while not listed in the table, correspond to (i.e., homologous to, i.e., which could be aligned in a statistically significant manner to) such mouse proteins or genes, and mouse proteins which are at least substantially  
10 identical or conservatively identical to the listed mouse proteins.

Related human genes (database DNAs) and proteins were identified by searching a database comprising human DNAs or  
15 proteins for sequences corresponding to (i.e., homologous to, i.e., which could be aligned in a statistically significant manner to) the mouse gene or protein. More than one human protein may be identified as corresponding to a particular mouse chip probe and to a particular mouse gene.

20       Note that the terms "human genes" and "human proteins" are used in a manner analogous to that already discussed in the case of "mouse genes" and "mouse proteins".

As used herein, the term "corresponding" does not mean identical, but rather implies the existence of a  
25 statistically significant sequence similarity, such as one sufficient to qualify the human protein or gene as a homologous protein or DNA as defined below. The greater the degree of relationship as thus defined (i.e., by the statistical significance of each alignment used to connect  
30 the mouse cDNA to the human protein or gene, measured by an E value), the more close the correspondence. The connection may be direct (mouse gene to human protein) or indirect (e.g., mouse gene to human gene, human gene to human protein). By "mouse gene", we mean the mouse gene from which  
35 the gene chip DNA in question was derived.

In general, the human genes/proteins which most closely correspond, directly or indirectly, to the mouse genes are preferred, such as the one(s) with the highest, top two

highest, top three highest, top four highest, top five highest, and top ten highest E values for the final alignment in the connection process. The human genes/proteins deemed to correspond to our mouse genes are identified in the Master Tables.

Note that it is possible to identify homologous full-length human genes and proteins, if they are present in the database, even if the query mouse DNA or protein sequence is not a full-length sequence.

If there is no homologous full-length human gene or protein in the database, but there is a partial one, the latter may nonetheless be useful. For example, a partial protein may still have biological activity, and a molecule which binds the partial protein may also bind the full-length protein so as to antagonize a biological activity of the full-length protein. Likewise, a partial human gene may encode a partial protein which has biological activity, or the gene may be useful in the design of a hybridization probe or in the design of a therapeutic antisense DNA.

The partial genes and protein sequences may of course also be used in the design of probes intended to identify the full length gene or protein sequence.

For the sake of convenience, we refer to a human protein as favorable if (1) it is listed in Master Table 1 as corresponding to a favorable mouse gene, or (2) it is at least substantially identical or conservatively identical to a listed protein per (1), or (3) it is a member of a human protein class listed in Master Table 2 (if provided) as corresponding to a favorable mouse gene. We define a human protein as unfavorable in an analogous manner. We may further identify a human protein as being wholly favorable (see mouse genes of subtable 1A, wholly unfavorable (see mouse genes of subtable 1B), or mixed, i.e., both partially favorable and partially unfavorable (see mouse genes of subtable 1C).

Likewise, a human gene which encodes a particular human protein may be classified in the same way as the human protein which it encodes.

However, it should be noted that this classification is not based on the direct study of the expression of the human gene/protein. of course, the human genes/proteins of ultimate interest will be the ones whose change in level of expression is, in fact, correlated, directly or inversely, with the change of state (normal, hyperinsulinemic, diabetic) of the subject.

After identifying related human genes and proteins, one may formulate agents useful in screening humans at risk for progression toward hyperinsulinemia or toward type II diabetes, or protecting humans at risk thereof from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

Agents which bind the "favorable" and "unfavorable" nucleic acids (e.g., the agent is a substantially complementary nucleic acid hybridization probe), or the corresponding proteins (e.g., an antibody vs. the protein) may be used to evaluate whether a human subject is at increased or decreased risk for progression toward type II diabetes. A subject with one or more elevated "unfavorable" and/or one or more depressed "favorable" genes/proteins is at increased risk, and one with one or more elevated "favorable" and/or one or more depressed "unfavorable" genes/proteins is at decreased risk. One may further take into account whether the subject is normoinsulinemic or hyperinsulinemic at the time of the assay. If the subject is non-diabetic and normoinsulinemic, we are especially interested in the "favorable" and "unfavorable" human genes/proteins corresponding to mouse genes differentially expressed in hyperinsulinemic vs. normal muscle. If the subject is already hyperinsulinemic, yet non-diabetic, we are especially interested in the "favorable" and "unfavorable" human genes/proteins corresponding to mouse genes differentially expressed in type II diabetic vs. hyperinsulinemic muscle.

The assay may be used as a preliminary screening assay to select subjects for further analysis, or as a formal diagnostic assay.

5           The identification of the related genes and proteins may also be useful in protecting humans against these disorders.

          Thus, Applicants contemplate:

          (1) use of the "favorable" mouse DNAs (or fragments  
10       thereof) of the Master Tables (below) to isolate or identify related human DNAs;

          (2) use of human DNAs, related to favorable mouse DNAs, to express the corresponding human proteins;

          (3) use of the corresponding human proteins (and mouse  
15       proteins, if biologically active in humans), to protect against the disorder(s);

          (4) use of the corresponding mouse or human proteins, or nucleic acid probes derived from the mouse or human genes, in diagnostic agents, in assays to measure  
20       progression toward hyperinsulinemia or type II diabetes, or protection against the disorder(s), or to estimate related end organ damage such as kidney damage; and

          (5) use of the corresponding human or mouse genes therapeutically in gene therapy, to protect against the  
25       disorder(s).

          Moreover Applicants contemplate:

          (1) use of the "unfavorable" mouse DNAs (or fragments thereof) of the Master Tables to isolate or identify related human DNAs;

30       (2) use of the complement to the "unfavorable" mouse DNAs or related human DNAs, as antisense molecules to inhibit expression of the related human DNAs;

          (3) use of the mouse or human DNAs to express the corresponding mouse or human proteins;

35       (4) use of the corresponding mouse or human proteins, in diagnostic agents, to measure progression toward hyperinsulinemia or type II diabetes, or protection against the disorder(s), or to estimate related end organ damage such as kidney damage;

(5) use of the corresponding mouse or human proteins in assays to determine whether a substance binds to (and hence may neutralize) the protein; and

5 (6) use of the neutralizing substance to protect against the disorder(s).

Thus, DNAs of interest include those which specifically hybridize to the aforementioned mouse or human genes, and are thus of interest as hybridization assay reagents or for  
10 antisense therapy. They also include synthetic DNA sequences which encode the same polypeptide as is encoded by the database DNA, and thus are useful for producing the polypeptide in cell culture or in situ (i.e., gene therapy). Moreover, they include DNA sequences which encode  
15 polypeptides which are substantially structurally identical or conservatively identical in amino acid sequence to the mouse and human proteins identified in the Master Table 1, subtables 1A or 1C. Finally, they include DNA sequences which encode peptide (including antibody) antagonists of the  
20 proteins of Master Table 1, subtables 1B or 1C.

The related human DNAs may be identified by comparing the mouse sequence (or its AA translation product) to known human DNAs (and their AA translation products).

25 Related human DNAs also may be identified by screening human cDNA or genomic DNA libraries using the mouse gene of the Master Table, or a fragment thereof, as a probe. If the mouse gene of Master Table 1 is not full-length, and there is no closely corresponding full-length mouse gene in  
30 the sequence databank, then the mouse DNA may first be used as a hybridization probe to screen a mouse cDNA library to isolate the corresponding full-length sequence. Alternatively, the mouse DNA may be used as a probe to screen a mouse genomic DNA library.

35 Our animal models of hyperinsulinemia and diabetes are also obese. It is possible that the genes found to be favorable act indirectly by inhibiting obesity. Likewise, it is possible that the genes found to be unfavorable act indirectly by accentuating obesity. Consequently, it is

within the compass of the present invention to use the favorable genes and proteins, or to use antagonists of the unfavorable genes and proteins, to protect against obesity, as well as against sequelae of obesity such as

5 hyperinsulinemia and diabetes.

Since type II diabetes is an age-related disease, the agents of the present invention may be used in conjunction with known anti-aging or anti-age-related disease agents. It is of particular interest to use the agents of the

10 present invention in conjunction with an agent disclosed in one of the related applications cited above, in particular, an antagonist to CIDE-A, the latter having been taught in Kopchick7 and Kopchick7A-PCT.

**BRIEF DESCRIPTION OF THE DRAWINGS**

**Figure 1.** Body weight gain [Fig. 1a], fasting glucose [Fig. 1b] and fasting insulin [Fig. 1c] levels of mice on the HF or Std diets.

5

**Figure 2.** Expression levels of Actin, alpha, cardiac (Actc1, NM\_009608) using RNA isolated from gastrocnemius muscle of individual diabetic HF mice and corresponding Std mice at different time points.

10

**Figure 3.** Data shown are expression levels for additional actin-related and actin-binding genes exhibiting a consistent decrease in expression in the HF mice in comparison to Std mice at all four time points (Fig. 3(a)) or at three of the four time points (Fig. 3(b)).

15



## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS OF THE INVENTION

### 5 Full-Length vs. Partial Length Genes/Proteins

A "full length" gene is here defined as (1) a naturally occurring DNA sequence which begins with an initiation codon (almost always the Met codon, ATG), and ends with a stop codon in phase with said initiation codon (when introns, if any, are ignored), and thereby encodes a naturally occurring polypeptide with biological activity, or a naturally occurring precursor thereof, or (2) a synthetic DNA sequence which encodes the same polypeptide as that which is encoded by (1). The gene may, but need not, include introns.

A "full-length" protein is here defined as a naturally occurring protein encoded by a full-length gene, or a protein derived naturally by post-translational modification of such a protein. Thus, it includes mature proteins, proproteins, preproteins and preproproteins. It also includes substitution and extension mutants of such naturally occurring proteins.

### Subjects

A mouse is considered to be a diabetic subject if, regardless of its fasting plasma insulin level, it has a fasting plasma glucose level of at least 190 mg/dL. A mouse is considered to be a hyperinsulinemic subject if its fasting plasma insulin level is at least 0.67 ng/mL and it does not qualify as a diabetic subject. A mouse is considered to be "normal" if it is neither diabetic nor hyperinsulinemic. Thus, normality is defined in a very limited manner.

A mouse is considered "obese" if its weight is at least 15% in excess of the mean weight for mice of its age and sex. A mouse which does not satisfy this standard may be characterized as "non-obese", the term "normal" being reserved for use in reference to glucose and insulin levels as previously described.

A human is considered a diabetic subject if, regardless of his or her fasting plasma insulin level, the fasting plasma glucose level is at least 126 mg/dL. A human is considered a hyperinsulinemic subject if the fasting plasma insulin level is more than 26 micro International Units/mL (it is believed that this is equivalent to 1.08 ng/mL), and does not qualify as a diabetic subject. A human is considered to be "normal" if it is neither diabetic nor hyperinsulinemic. Thus, normality is defined in a very limited manner.

A human is considered "obese" if the body mass index (BMI) (weight divided by height squared) is at least 30 kg/m<sup>2</sup>. A human who does not satisfy this standard may be characterized as "non-obese", the term "normal" being reserved for use in reference to glucose and insulin levels as previously described.

A human is considered overweight if the BMI is at least 25 kg/m<sup>2</sup>. Thus, we define overweight to include obese individuals, consistent with the recommendations of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). A human who does not satisfy this standard may be characterized as "non-overweight."

According to the Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, Diabetes Care 20: 1183-97 (1997), the following are risk factors for diabetes type II:

older (e.g., at least 45; see below)

excessive weight (see below)

first-degree relative with diabetes mellitus

member of high risk ethnic group (black, Hispanic, Native American, Asian)

history of gestational diabetes mellitus or delivering a baby weighing more than 9 pounds (4.032 kg)

36

hypertensive (>140/90 mm Hg)

HDL cholesterol level >35 mg/dL (0.90 mmol/L)

5       triglyceride level >=250 mg/dL (2.83 mmol/L)

Hence, in a preferred embodiment, the diagnostic and protective methods of the present invention are applied to human subjects exhibiting one or more of the aforementioned risk factors. Likewise, in a preferred embodiment, they are applied to human subjects who, while not diabetic, exhibit impaired glucose homeostasis (110 to <126 mg/dL).

The risk of diabetes increases with age. Hence, in successive preferred embodiments, the age of the subjects is at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, and at least 75.

With regard to excessive weight, NIDDK says that "The relative risk of diabetes increases by approximately 25 percent for each additional unit of BMI over 22." Hence, in successive preferred embodiments, the BMIs of the human subjects is at least 23, at least 24, at least 25 (i.e., overweight by our criterion), at least 26, at least 27, at least 28, at least 29, at least 30 (i.e., obese), at least 31, at least 32, at least 33, at least 34, at least 35, at least 36, at least 37, at least 38, at least 39, at least 40, or over 40.

#### **Age-Related Diseases**

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Age-related (senescent) diseases include certain cancers, atherosclerosis, diabetes (type 2), osteoporosis, hypertension, depression, Alzheimer's, Parkinson's, glaucoma, certain immune system defects, kidney failure, and liver steatosis. In general, they are diseases for which the relative risk (comparing a subpopulation over age 55 to a suitably matched population under age 55) is at least 1.1.

Preferably, the agents of the present invention protect against one or more age-related diseases for at least a subpopulation of mature (post-puberty) adult subjects.

5

#### **Direct and Indirect Utility of Identified Nucleic Acid Sequences and Related Molecules**

The mouse or human genes (or fragments thereof) may be used directly. For diagnostic or screening purposes, they (or specific binding fragments thereof) may be labeled and used as hybridization probes. For therapeutic purposes, they (or specific binding fragments thereof) may be used as antisense reagents to inhibit the expression of the corresponding gene, or of a sufficiently homologous gene of another species.

If the database DNA appears to be a full-length cDNA or gDNA, that is, it encodes an entire, functional, naturally occurring protein, then it may be used in the expression of that protein. Likewise, if the corresponding human gene is known in full-length, it may be used to express the human protein. Such expression may be in cell culture, with the protein subsequently isolated and administered exogenously to subjects who would benefit therefrom, or in vivo, i.e., administration by gene therapy. Naturally, any DNA encoding the same protein may be used for the same purpose, and a DNA encoding a protein which a fragment or a mutant of that naturally occurring protein which retains the desired activity, may be used for the purpose of producing the active fragment or mutant. The encoded protein of course has utility therapeutically and, in labeled or immobilized form, diagnostically.

The genes may also be used indirectly, that is, to identify other useful DNAs, proteins, or other molecules. We have attempted to determine whether the mouse genes disclosed herein have significant similarity to any known human DNA, and whether, in any of the six possible combinations of reference frame and strand, they encode a protein similar to a known human protein. If so, then it

follows that the known human protein, and DNAs encoding that protein, may be used in a similar manner. In addition, if the known human protein is known to have additional homologues, then those homologous proteins, and DNAs encoding them, may be used in a similar manner.

There thus are several ways that a human protein homologue of interest can be identified by database searching, including but not limited to:

- 1) a DNA->DNA (BlastN) search for human database DNAs closely related to the mouse gene identifies a known human gene, and the sequence of the human protein is deduced by the Genetic Code;
- 2) a DNA->Protein (BlastX) search for human database proteins closely related to the translated DNA of the mouse gene identifies a known human protein; and
- 3) the sequence of the mouse protein is known or is deduced by the Genetic Code, and a Protein->Protein (BlastP) search for closely related database proteins identifies a known human protein.

Once a known human gene is identified, it may be used in further BlastN or BlastX searches to identify other human genes or proteins. Once a known human protein is identified, it may be used in further BlastP searches to identify other human proteins.

Searches may also take cognizance, intermediately, of known genes and proteins other than mouse or human ones, e.g., use the mouse sequence to identify a known rat sequence and then the rat sequence to identify a human one.

If we have identified a mouse gene, and it encodes a mouse protein which appears similar to a human protein, then that human protein may be used (especially in humans) for

purposes analogous to the proposed use of the mouse protein in mice. Moreover, a specific binding fragment of an appropriate strand of the corresponding human gene (gDNA or cDNA) could be labeled and used as a hybridization probe (especially against samples of human mRNA or cDNA).

In determining whether the disclosed genes (gDNA or cDNA) have significant similarities to known DNAs (and their translated AA sequences to known proteins), one would generally use the disclosed gene as a query sequence in a search of a sequence database. The results of several such searches are set forth in the Examples. Such results are dependent, to some degree, on the search parameters. Preferred parameters are set forth in Example 1. The results are also dependent on the content of the database. While the raw similarity score of a particular target (database) sequence will not vary with content (as long as it remains in the database), its informational value (in bits), expected value, and relative ranking can change. Generally speaking, the changes are small.

It will be appreciated that the nucleic acid and protein databases keep growing. Hence a later search may identify high scoring target sequences which were not uncovered by an earlier search because the target sequences were not previously part of a database.

Hence, in a preferred embodiment, the cognate DNAs and proteins include not only those set forth in the examples, but those which would have been highly ranked (top ten, more preferably top three, even more preferably top two, most preferably the top one) in a search run with the same parameters on the date of filing of this application.

If the known mouse or human database DNA appears to be a partial sequence (that is, partial relative to a cDNA or gDNA encoding the whole naturally occurring protein), it may be used as a hybridization probe to isolate the full-length DNA. If the partial DNA encodes a biologically functional fragment of the cognate protein, it may be used in a manner

similar to the full length DNA, i.e., to produce the functional fragment.

If we have indicated that an antagonist of a protein or other molecule is useful, then such an antagonist may be obtained by preparing a combinatorial library, as described below, of potential antagonists, and screening the library members for binding to the protein or other molecule in question. The binding members may then be further screened for the ability to antagonize the biological activity of the target. The antagonists may be used therapeutically, or, in suitably labeled or immobilized form, diagnostically.

If the identified mouse or human database DNA is related to a known protein, then substances known to interact with that protein (e.g., agonists, antagonists, substrates, receptors, second messengers, regulators, and so forth), and binding molecules which bind them, are also of utility. Such binding molecules can likewise be identified by screening a combinatorial library.

#### **Isolation of Full Length DNAs Using Partial DNAs as probes**

If it is determined that a DNA of the present invention is a partial DNA, and the cognate full length DNA is not listed in a sequence database, the available DNA may be used as a hybridization probe to isolate the full-length DNA from a suitable DNA library.

Stringent hybridization conditions are appropriate, that is, conditions in which the hybridization temperature is 5-10 deg. C. below the  $T_m$  of the DNA as a perfect duplex.

#### **Identification and Isolation of Homologous Genes Using a DNA Probe**

It may be that the sequence databases available do not include the sequence of any homologous gene (cDNA or gDNA), or at least of the homologous gene for a species of interest. However, given the cDNAs set forth above, one may readily obtain the homologous gene.

The possession of one DNA (the "starting DNA") greatly facilitates the isolation of homologous DNAs. If only a

partial DNA is known, this partial DNA may first be used as a probe to isolate the corresponding full length DNA for the same species, and that the latter may be used as the starting DNA in the search for homologous genes.

5       The starting DNA, or a fragment thereof, is used as a hybridization probe to screen a cDNA or genomic DNA library for clones containing inserts which encode either the entire homologous protein, or a recognizable fragment thereof. The minimum length of the hybridization probe is dictated by the  
10       need for specificity. If the size of the library in bases is  $L$ , and the GC content is 50%, then the probe should have a length of at least  $l$ , where  $L = 4^l$ . This will yield, on average, a single perfect match in random DNA of  $L$  bases. The human cDNA library is about  $10^8$  bases and the human  
15       genomic DNA library is about  $10^{10}$  bases.

      The library is preferably derived from an organism which is known, on biochemical evidence, to produce a homologous protein, and more preferably from the genomic DNA or mRNA of cells of that organism which are likely to be  
20       relatively high producers of that protein. A cDNA library (which is derived from an mRNA library) is especially preferred.

      If the organism in question is known to have substantially different codon preferences from that of the  
25       organism whose relevant cDNA or genomic DNA is known, a synthetic hybridization probe may be used which encodes the same amino acid sequence but whose codon utilization is more similar to that of the DNA of the target organism. Alternatively, the synthetic probe may employ inosine as a  
30       substitute for those bases which are most likely to be divergent, or the probe may be a mixed probe which mixes the codons for the source DNA with the preferred codons (encoding the same amino acid) for the target organism.

      By routine methods, the  $T_m$  of a perfect duplex of  
35       starting DNA is determined. One may then select a hybridization temperature which is sufficiently lower than the perfect duplex  $T_m$  to allow hybridization of the starting DNA (or other probe) to a target DNA which is divergent from the starting DNA. A 1% sequence divergence typically lowers



the  $T_m$  of a duplex by 1-2°C, and the DNAs encoding homologous proteins of different species typically have sequence identities of around 50-80%. Preferably, the library is screened under conditions where the temperature is at least 20°C., more preferably at least 50°C., below the perfect duplex  $T_m$ . Since salt reduces the  $T_m$ , one ordinarily would carry out the search for DNAs encoding highly homologous proteins under relatively low salt hybridization conditions, e.g., <1M NaCl. The higher the salt concentration, and/or the lower the temperature, the greater the sequence divergence which is tolerated.

For the use of probes to identify homologous genes in other species, see, e.g., Schwinn, et al., J. Biol. Chem., 265:8183-89 (1990) (hamster 67-bp cDNA probe vs. human leukocyte genomic library; human 0.32kb DNA probe vs. bovine brain cDNA library, both with hybridization at 42°C in 6xSSC); Jenkins et al., J. Biol. Chem., 265:19624-31 (1990) (Chicken 770-bp cDNA probe vs. human genomic libraries; hybridization at 40°C in 50% formamide and 5xSSC); Murata et al., J. Exp. Med., 175:341-51 (1992) (1.2-kb mouse cDNA probe v. human eosinophil cDNA library; hybridization at 65°C in 6xSSC); Guyer et al., J. Biol. Chem., 265:17307-17 (1990) (2.95-kb human genomic DNA probe vs. porcine genomic DNA library; hybridization at 42°C in 5xSSC). The conditions set forth in these articles may each be considered suitable for the purpose of isolating homologous genes.

#### **Corresponding (Homologous) Proteins and DNAs**

In the case of a gene chip, the manufacturer of the gene chip determines which DNA to place at each position on the chip. This DNA may correspond in sequence to a genomic DNA, a cDNA, or a fragment of genomic or cDNA, and may be natural, synthetic or partially natural and partially synthetic in origin. The manufacturer of the gene chip will normally identify the DNA for a mouse gene chip as corresponding to a particular mouse gene, in which case it will be assumed that the alignments of chip DNA to mouse gene satisfies the homology criteria of the invention.

Usually, the gene chip manufacturer will provide a sequence database accession number for the mouse DNA. If so, to identify the corresponding mouse protein, we will first inspect the database record for that mouse DNA. Often, the mouse protein accession number will appear in that record or in a linked record. If it doesn't, the corresponding mouse protein can be identified by performing a BlastX search on a mouse protein database with the mouse database DNA sequence as the query sequence. Even if the protein sequence is not in the database, if the DNA sequence comprises a full-length coding sequence, the corresponding protein can be identified by translating the coding sequence in accordance with the Genetic Code.

A human protein can be said to be identifiable as corresponding (homologous) to a gene chip DNA if it is identified as corresponding (homologous) to the mouse gene (gDNA or cDNA, whole or partial) identified by the gene chip manufacturer as corresponding to that gene chip DNA.

In turn, it is identifiable as corresponding (homologous) to said identified mouse gene, if

(1) it can be aligned by BlastX directly to that **mouse gene**, and/or

(2) it is encoded by a **human gene**, or can be aligned to a **human gene** by BlastX, which in turn can be aligned by BlastN to said mouse gene and/or

(3) it can be aligned by BlastP to a **mouse protein**, the latter being encoded by said mouse gene, or aligned to said mouse gene BlastX,

where any alignment by BlastN, BlastP or BlastX is in accordance with the default parameters set forth below, and the expected value (E) of each alignment (the probability that such an alignment would have occurred by chance alone)

is less than  $e^{-10}$ . (Note that because this is a negative exponent, a value such as  $e^{-50}$  is less than  $e^{-10}$ .)

Desirably, two or all three of these conditions (1)-(3) are satisfied for the corresponding (homologous) human genes and proteins.

A human gene is corresponding (homologous) to a mouse gene chip DNA, and hence to said identified mouse gene (or cDNA) and protein, if it encodes a corresponding (homologous) human protein as defined above, or it can be aligned by BlastN to said mouse gene.

Preferably, for at least one of conditions (1)-(3), the E value is less than  $e^{-50}$ , more preferably less than  $e^{-60}$ , still more preferably less than  $e^{-70}$ , even more preferably less than  $e^{-80}$ , considerably more preferably less than  $e^{-90}$ , and most preferably less than  $e^{-100}$ . Desirably, it is true for two or even all three of these conditions.

In constructing Master table 1, we generally used a BlastX (mouse gene vs. human protein) alignment E value cutoff of  $e^{-50}$ . However, if there were no human proteins with that good an alignment to the mouse DNA in question, or if there were other reasons for including a particular human protein (e.g., a known functionality supportive of the observed differential cognate mouse protein expression), then a human protein with a score worse (i.e., higher) than  $e^{-50}$  may appear in Master Table 1.

If the manufacturer of the gene chip identifies the gene chip DNA as corresponding to an EST, or other DNA which is not a full-length mouse gene or cDNA, a longer (possibly full length) mouse gene or cDNA may be identified by a BlastN search of the mouse DNA database. Alternatively, the identified DNA may be used to conduct a BlastN search of a human DNA database, or a BlastX search of a mouse or human protein database.

Thus, more generally, a human protein can be said to be identifiable as corresponding (homologous) to a gene chip

DNA, or to a DNA identified by the manufacturer as corresponding to that gene chip DNA, if

(1') it can be aligned directly to the gene chip or  
5 corresponding manufacturer identified DNA by BlastX. and/or

(2') it can be aligned to a human gene/cDNA by BlastX, whose  
genomic DNA (gDNA) or cDNA (DNA complementary to messenger  
RNA) in turn can be aligned to the gene chip or  
10 corresponding manufacturer identified DNA by BlastN, and/or

(3') it can be aligned to a mouse gene/cDNA by BlastX, whose  
gDNA or cDNA in turn can be aligned to the gene chip or  
corresponding manufacturer identified DNA by BlastN, and/or  
15

(4') it can be aligned to a mouse protein by BlastP, which  
in turn can be aligned to the gene chip or corresponding  
manufacturer identified DNA by BlastX, and/or

(5') it can be aligned to a mouse protein by BlastP, which  
in turn can be aligned to a mouse gene/cDNA by BlastX, whose  
gDNA or cDNA can in turn be aligned to the gene chip or  
corresponding manufacturer identified DNA by BlastN;  
20

where any alignment by BlastN, BlastP, or BlastX is in  
accordance with the default parameters set forth below, and  
the expected value (E) of each alignment (the probability  
that such an alignment would have occurred by chance alone)  
is less than  $e^{-10}$ . (Note that because this is a negative  
exponent, a value such as  $e^{-50}$  is less than  $e^{-10}$ .)  
25  
30

Preferably, two, three, four or all five of conditions  
(1')-(5') are satisfied.

Preferably, for at least one of conditions (1')-(5'),  
35 for at least the final alignment (i.e., vs. the human  
protein), the E value is less than  $e^{-50}$ , more preferably  
less than  $e^{-60}$ , , still more preferably less than  $e^{-70}$ , even  
more preferably less than  $e^{-80}$ , considerably more preferably  
less than  $e^{-90}$ , and most preferably less than  $e^{-100}$ .

Desirably, one or more of these standards of preference are met for two, three, four or all five of conditions (1')-(5'). In particular, for those conditions in which the gene chip or corresponding manufacturer identified DNA is indirectly connected to the human protein by virtue of two or more successive alignments, the E value is preferably, so limited for all of said alignments in the connecting chain.

A human gene corresponds (is homologous) to a gene chip DNA or manufacturer identified corresponding DNA if it encodes a homologous human protein as defined above, or if it can be aligned either directly to that DNA, or indirectly through a mouse gene which can be aligned to said DNA, according to the conditions set forth above.

Master table 1 assembles a list of human protein corresponding to each of the mouse DNAs/proteins identified as related to the chip DNA. These human proteins form a set and can be given a percentile rank, with respect to E value, within that set. The human proteins of the present invention preferably are those scorers with a percentile rank of at least 50%, more preferably at least 60%, still more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90%.

For each mouse gene (gDNA or cDNA) in Master Table 1, there is a particular human protein which provides the best alignment match as measured by BlastX, i.e., the human protein with the best score (lowest e-value). These human proteins form a subset of the set above and can be given a percentile rank within that subset, e.g., the human proteins with scores in the top 10% of that subset have a percentile rank of 90% or higher.

The human proteins of the present invention preferably are those best scorer subset proteins with a percentile rank within the subset of at least 50%, more preferably at least 60%, still more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90%.

BlastN and BlastX report very low expected values as "0.0". This does not truly mean that the expected value is exactly zero (since any alignment could occur by chance), but merely that it is so infinitesimal that it is not reported. The documentation does not state the cutoff value, but alignments with explicit E values as low as  $e^{-178}$  (624 bits) have been reported as nonzero values, while a score of 636 bits was reported as "0.0".

Functionally homologous human proteins are also of interest. A human protein may be said to be functionally homologous to the mouse gene if the human protein has at least one biological activity in common with the mouse protein encoded by said mouse gene.

The human proteins of interest also include those that are substantially and/or conservatively identical (as defined below) to the homologous and/or functionally homologous human proteins defined above.

#### **Degree of Differential Expression**

The degree of differential expression may be expressed as the ratio of the higher expression level to the lower expression level. Preferably, this is at least 2-fold, and more preferably, it is higher, such as at least 3-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 7-fold, at least 8-fold, at least 9-fold, or at least 10-fold.

Most preferably, the human protein of interest corresponds to a mouse gene for which the degree of differential expression places it among the top 10% of the mouse genes in the appropriate subtable.

#### **Relevance of Favorable and Unfavorable Genes**

If a gene is down-regulated in more favored mammals, or up-regulated in less favored mammals, (i.e., an "unfavorable gene") then several utilities are apparent.

5 First, the complementary strand of the gene, or a portion thereof, may be used in labeled form as a hybridization probe to detect messenger RNA and thereby monitor the level of expression of the gene in a subject. Elevated levels are indicative of progression, or propensity to progression, to a less favored state, and  
10 clinicians may take appropriate preventative, curative or ameliorative action.

Secondly, the messenger RNA product (or equivalent cDNA), the protein product, or a binding molecule specific for that product (e.g., an antibody which binds the  
15 product), or a downstream product which mediates the activity (e.g., a signaling intermediate) or a binding molecule (e.g., an antibody) therefor, may be used, preferably in labeled or immobilized form, as an assay reagent in an assay for said nucleic acid product, protein  
20 product, or downstream product (e.g., a signaling intermediate). Again, elevated levels are indicative of a present or future problem.

Thirdly, an agent which down-regulates expression of the gene may be used to reduce levels of the corresponding  
25 protein and thereby inhibit further damage. This agent could inhibit transcription of the gene in the subject, or translation of the corresponding messenger RNA. Possible inhibitors of transcription and translation include antisense molecules and repressor molecules. The agent  
30 could also inhibit a post-translational modification (e.g., glycosylation, phosphorylation, cleavage, GPI attachment) required for activity, or post-translationally modify the protein so as to inactivate it. Or it could be an agent which down- or up-regulated a positive or negative  
35 regulatory gene, respectively.

Fourthly, an agent which is an antagonist of the messenger RNA product or protein product of the gene, or of a downstream product through which its activity is

manifested (e.g., a signaling intermediate), may be used to inhibit its activity.

This antagonist could be an antibody, a peptide, a peptoid, a nucleic acid, a peptide nucleic acid (PNA) oligomer, a small organic molecule of a kind for which a combinatorial library exists (e.g., a benzodiazepine), etc. An antagonist is simply a binding molecule which, by binding, reduces or abolishes the undesired activity of its target. The antagonist, if not an oligomeric molecule, is preferably less than 1000 daltons, more preferably less than 500 daltons.

Fifthly, an agent which degrades, or abets the degradation of, that messenger RNA, its protein product or a downstream product which mediates its activity (e.g., a signaling intermediate), may be used to curb the effective period of activity of the protein.

If a gene is up-regulated in more favored mammals, or down-regulated in less favored animals then the utilities are converse to those stated above.

First, the complementary strand of the gene, or a portion thereof, may be used in labeled form as a hybridization probe to detect messenger RNA and thereby monitor the level of expression of the gene in a subject. Depressed levels are indicative of damage, or possibly of a propensity to damage, and clinicians may take appropriate preventative, curative or ameliorative action.

Secondly, the messenger RNA product, the equivalent cDNA, protein product, or a binding molecule specific for those products, or a downstream product, or a signaling intermediate, or a binding molecule therefor, may be used, preferably in labeled or immobilized form, as an assay reagent in an assay for said protein product or downstream product. Again, depressed levels are indicative of a present or future problem.

Thirdly, an agent which up-regulates expression of the gene may be used to increase levels of the corresponding protein and thereby inhibit further progression to a less favored state. By way of example, it could be a vector which carries a copy of the gene, but which expresses the



gene at higher levels than does the endogenous expression system. Or it could be an agent which up- or down-regulates a positive or negative regulatory gene.

Fourthly, an agent which is an agonist of the protein product of the gene, or of a downstream product through which its activity (of inhibition of progression to a less favored state) is manifested, or of a signaling intermediate may be used to foster its activity.

Fifthly, an agent which inhibits the degradation of that protein product or of a downstream product or of a signaling intermediate may be used to increase the effective period of activity of the protein.

#### **Mutant Proteins**

The present invention also contemplates mutant proteins (peptides) which are substantially identical (as defined below) to the parental protein (peptide). In general, the fewer the mutations, the more likely the mutant protein is to retain the activity of the parental protein. The effect of mutations is usually (but not always) additive. Certain individual mutations are more likely to be tolerated than others.

A protein is more likely to tolerate a mutation which

(a) is a substitution rather than an insertion or deletion;

(b) is an insertion or deletion at the terminus, rather than internally, or, if internal, is at a domain boundary, or a loop or turn, rather than in an alpha helix or beta strand;

(c) affects a surface residue rather than an interior residue;

(d) affects a part of the molecule distal to the binding site;

(e) is a substitution of one amino acid for another of similar size, charge, and/or hydrophobicity, and does not destroy a disulfide bond or other crosslink; and

(f) is at a site which is subject to substantial variation among a family of homologous proteins to which the protein of interest belongs.

These considerations can be used to design functional mutants.

#### *Surface vs. Interior Residues*

Charged amino acid residues almost always lie on the surface of the protein. For uncharged residues, there is less certainty, but in general, hydrophilic residues are partitioned to the surface and hydrophobic residues to the interior. Of course, for a membrane protein, the membrane-spanning segments are likely to be rich in hydrophobic residues.

Surface residues may be identified experimentally by various labeling techniques, or by 3-D structure mapping techniques like X-ray diffraction and NMR. A 3-D model of a homologous protein can be helpful.

#### *Binding Site Residues*

Residues forming the binding site may be identified by (1) comparing the effects of labeling the surface residues before and after complexing the protein to its target, (2) labeling the binding site directly with affinity ligands, (3) fragmenting the protein and testing the fragments for binding activity, and (4) systematic mutagenesis (e.g., alanine-scanning mutagenesis) to determine which mutants destroy binding. If the binding site of a homologous protein is known, the binding site may be postulated by analogy.

Protein libraries may be constructed and screened that a large family (e.g.,  $10^6$ ) of related mutants may be evaluated simultaneously.

Hence, the mutations are preferably conservative modifications as defined below.

#### *"Substantially Identical"*

A mutant protein (peptide) is substantially identical to a reference protein (peptide) if (a) it has at least 10%

of a specific binding activity or a non-nutritional biological activity of the reference protein, and (b) is at least 50% identical in amino acid sequence to the reference protein (peptide). It is "substantially structurally identical" if condition (b) applies, regardless of (a).

Percentage amino acid identity is determined by aligning the mutant and reference sequences according to a rigorous dynamic programming algorithm which globally aligns their sequences to maximize their similarity, the similarity being scored as the sum of scores for each aligned pair according to an unbiased PAM250 matrix, and a penalty for each internal gap of -12 for the first null of the gap and -4 for each additional null of the same gap. The percentage identity is the number of matches expressed as a percentage of the adjusted (i.e., counting inserted nulls) length of the reference sequence.

A mutant DNA sequence is substantially identical to a reference DNA sequence if they are structural sequences, and encoding mutant and reference proteins which are substantially identical as described above.

If instead they are regulatory sequences, they are substantially identical if the mutant sequence has at least 10% of the regulatory activity of the reference sequence, and is at least 50% identical in nucleotide sequence to the reference sequence. Percentage identity is determined as for proteins except that matches are scored +5, mismatches -4, the gap open penalty is -12, and the gap extension penalty (per additional null) is -4.

More preferably, the sequence is not merely substantially identical but rather is at least 51%, at least 66%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical in sequence to the reference sequence.

DNA sequences may also be considered "substantially identical" if they hybridize to each other under stringent conditions, i.e., conditions at which the  $T_m$  of the heteroduplex of the one strand of the mutant DNA and the more complementary strand of the reference DNA is not in

excess of 10°C. less than the  $T_m$  of the reference DNA homoduplex. Typically this will correspond to a percentage identity of 85-90%.

5 "Conservative Modifications"

"Conservative modifications" are defined as

(a) conservative substitutions of amino acids as hereafter defined; or

10 (b) single or multiple insertions (extension) or deletions (truncation) of amino acids at the termini.

Conservative modifications are preferred to other modifications. Conservative substitutions are preferred to other conservative modifications.

15 "Semi-Conservative Modifications" are modifications which are not conservative, but which are (a) semi-conservative substitutions as hereafter defined; or (b) single or multiple insertions or deletions internally, but at interdomain boundaries, in loops or in other segments of  
20 relatively high mobility. Semi-conservative modifications are preferred to nonconservative modifications. Semi-conservative substitutions are preferred to other semi-conservative modifications.

25 Non-conservative substitutions are preferred to other non-conservative modifications.

The term "conservative" is used here in an a priori sense, i.e., modifications which would be expected to preserve 3D structure and activity, based on analysis of the naturally occurring families of homologous proteins and of  
30 past experience with the effects of deliberate mutagenesis, rather than post facto, a modification already known to conserve activity. Of course, a modification which is conservative a priori may, and usually is, also conservative post facto.

35 Preferably, except at the termini, no more than about five amino acids are inserted or deleted at a particular locus, and the modifications are outside regions known to contain binding sites important to activity.

Preferably, insertions or deletions are limited to the termini.

A conservative substitution is a substitution of one amino acid for another of the same exchange group, the exchange groups being defined as follows

- I Gly, Pro, Ser, Ala (Cys) (and any nonbiogenic, neutral amino acid with a hydrophobicity not exceeding that of the aforementioned a.a.'s)
- II Arg, Lys, His (and any nonbiogenic, positively-charged amino acids)
- III Asp, Glu, Asn, Gln (and any nonbiogenic negatively-charged amino acids)
- IV Leu, Ile, Met, Val (Cys) (and any nonbiogenic, aliphatic, neutral amino acid with a hydrophobicity too high for I above)
- V Phe, Trp, Tyr (and any nonbiogenic, aromatic neutral amino acid with a hydrophobicity too high for I above).

Note that Cys belongs to both I and IV.

Residues Pro, Gly and Cys have special conformational roles. Cys participates in formation of disulfide bonds. Gly imparts flexibility to the chain. Pro imparts rigidity to the chain and disrupts  $\alpha$  helices. These residues may be essential in certain regions of the polypeptide, but substitutable elsewhere.

One, two or three conservative substitutions are more likely to be tolerated than a larger number.

"Semi-conservative substitutions" are defined herein as being substitutions within supergroup I/II/III or within supergroup IV/V, but not within a single one of groups I-V. They also include replacement of any other amino acid with alanine. If a substitution is not conservative, it preferably is semi-conservative.

"Non-conservative substitutions" are substitutions which are not "conservative" or "semi-conservative".

"Highly conservative substitutions" are a subset of conservative substitutions, and are exchanges of amino acids within the groups Phe/Tyr/Trp, Met/Leu/Ile/Val, His/Arg/Lys, Asp/Glu and Ser/Thr/Ala. They are more likely to be

tolerated than other conservative substitutions. Again, the smaller the number of substitutions, the more likely they are to be tolerated.

5 "Conservatively Identical"

A protein (peptide) is conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by conservative modifications, the protein (peptide) remaining at least seven amino acids long if the  
10 reference protein (peptide) was at least seven amino acids long.

A protein is at least semi-conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by semi-conservative or conservative  
15 modifications.

A protein (peptide) is nearly conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by one or more conservative modifications and/or a single nonconservative substitution.

20 It is highly conservatively identical if it differs, if at all, solely by highly conservative substitutions. Highly conservatively identical proteins are preferred to those merely conservatively identical. An absolutely identical protein is even more preferred.

25

The core sequence of a reference protein (peptide) is the largest single fragment which retains at least 10% of a particular specific binding activity, if one is specified, or otherwise of at least one specific binding activity of  
30 the referent. If the referent has more than one specific binding activity, it may have more than one core sequence, and these may overlap or not.

If it is taught that a peptide of the present invention  
35 may have a particular similarity relationship (e.g., markedly identical) to a reference protein (peptide), preferred peptides are those which comprise a sequence having that relationship to a core sequence of the reference protein (peptide), but with internal insertions or deletions

in either sequence excluded. Even more preferred peptides are those whose entire sequence has that relationship, with the same exclusion, to a core sequence of that reference protein (peptide).

5

### Library

The term "library" generally refers to a collection of chemical or biological entities which are related in origin, structure, and/or function, and which can be screened  
10 simultaneously for a property of interest.

Libraries may be classified by how they are constructed (natural vs. artificial diversity; combinatorial vs. noncombinatorial), how they are screened (hybridization,  
15 expression, display), or by the nature of the screened library members (peptides, nucleic acids, etc.).

In a "natural diversity" library, essentially all of the diversity arose without human intervention. This would be true, for example, of messenger RNA extracted from a non-engineered cell.  
20

In a "synthetic diversity" library, essentially all of the diversity arose deliberately as a result of human intervention. This would be true for example of a combinatorial library; note that a small level of natural  
25 diversity could still arise as a result of spontaneous mutation. It would also be true of a noncombinatorial library of compounds collected from diverse sources, even if they were all natural products.

In a "non-natural diversity" library, at least some of the diversity arose deliberately through human intervention.  
30

In a "controlled origin" library, the source of the diversity is limited in some way. A limitation might be to cells of a particular individual, to a particular species, or to a particular genus, or, more complexly, to individuals  
35 of a particular species who are of a particular age, sex, physical condition, geographical location, occupation and/or familial relationship. Alternatively or additionally, it might be to cells of a particular tissue or organ. Or it could be cells exposed to particular pharmacological,

environmental, or pathogenic conditions. Or the library could be of chemicals, or a particular class of chemicals, produced by such cells.

In a "controlled structure" library, the library members are deliberately limited by the production conditions to particular chemical structures. For example, if they are oligomers, they may be limited in length and monomer composition, e.g. hexapeptides composed of the twenty genetically encoded amino acids.

#### Hybridization Library

In a hybridization library, the library members are nucleic acids, and are screened using a nucleic acid hybridization probe. Bound nucleic acids may then be amplified, cloned, and/or sequenced.

#### Expression Library

In an expression library, the screened library members are gene expression products, but one may also speak of an underlying library of genes encoding those products. The library is made by subcloning DNA encoding the library members (or portions thereof) into expression vectors (or into cloning vectors which subsequently are used to construct expression vectors), each vector comprising an expressible gene encoding a particular library member, introducing the expression vectors into suitable cells, and expressing the genes so the expression products are produced.

In one embodiment, the expression products are secreted, so the library can be screened using an affinity reagent, such as an antibody or receptor. The bound expression products may be sequenced directly, or their sequences inferred by, e.g., sequencing at least the variable portion of the encoding DNA.

In a second embodiment, the cells are lysed, thereby exposing the expression products, and the latter are screened with the affinity reagent.

In a third embodiment, the cells express the library members in such a manner that they are displayed on the



surface of the cells, or on the surface of viral particles produced by the cells. (See display libraries, below).

In a fourth embodiment, the screening is not for the ability of the expression product to bind to an affinity reagent, but rather for its ability to alter the phenotype of the host cell in a particular detectable manner. Here, the screened library members are transformed cells, but there is a first underlying library of expression products which mediate the behavior of the cells, and a second underlying library of genes which encode those products.

#### Display Library

In a display library, the library members are each conjugated to, and displayed upon, a support of some kind. The support may be living (a cell or virus), or nonliving (e.g., a bead or plate).

If the support is a cell or virus, display will normally be effectuated by expressing a fusion protein which comprises the library member, a carrier moiety allowing integration of the fusion protein into the surface of the cell or virus, and optionally a lining moiety. In a variation on this theme, the cell coexpresses a first fusion comprising the library member and a linking moiety L1, and a second fusion comprising a linking moiety L2 and the carrier moiety. L1 and L2 interact to associate the first fusion with the second fusion and hence, indirectly, the library member with the surface of the cell or virus.

#### Soluble Library

In a soluble library, the library members are free in solution. A soluble library may be produced directly, or one may first make a display library and then release the library members from their supports.

#### Encapsulated Library

In an encapsulated library, the library members are inside cells or liposomes. Generally speaking, encapsulated libraries are used to store the library members for future use; the members are extracted in some way for screening

purposes. However, if they differentially affect the phenotype of the cells, they may be screened indirectly by screening the cells.

## 5 cDNA Library

A cDNA library is usually prepared by extracting RNA from cells of particular origin, fractionating the RNA to isolate the messenger RNA (mRNA has a poly(A) tail, so this is usually done by oligo-dT affinity chromatography),  
10 synthesizing complementary DNA (cDNA) using reverse transcriptase, DNA polymerase, and other enzymes, subcloning the cDNA into vectors, and introducing the vectors into cells. Often, only mRNAs or cDNAs of particular sizes will be used, to make it more likely that the cDNA encodes a  
15 functional polypeptide.

A cDNA library explores the natural diversity of the transcribed DNAs of cells from a particular source. It is not a combinatorial library.

A cDNA library may be used to make a hybridization  
20 library, or it may be used as an (or to make) expression library.

## Genomic DNA Library

A genomic DNA library is made by extracting DNA from a  
25 particular source, fragmenting the DNA, isolating fragments of a particular size range, subcloning the DNA fragments into vectors, and introducing the vectors into cells.

Like a cDNA library, a genomic DNA library is a natural diversity library, and not a combinatorial library. A  
30 genomic DNA library may be used the same way as a cDNA library.

## Synthetic DNA library

A synthetic DNA library may be screened directly (as a  
35 hybridization library), or used in the creation of an expression or display library of peptides/proteins.

## Combinatorial Libraries

The term "combinatorial library" refers to a library in which the individual members are either systematic or random combinations of a limited set of basic elements, the properties of each member being dependent on the choice and location of the elements incorporated into it. Typically, the members of the library are at least capable of being screened simultaneously. Randomization may be complete or partial; some positions may be randomized and others predetermined, and at random positions, the choices may be limited in a predetermined manner. The members of a combinatorial library may be oligomers or polymers of some kind, in which the variation occurs through the choice of monomeric building block at one or more positions of the oligomer or polymer, and possibly in terms of the connecting linkage, or the length of the oligomer or polymer, too. Or the members may be nonoligomeric molecules with a standard core structure, like the 1,4-benzodiazepine structure, with the variation being introduced by the choice of substituents at particular variable sites on the core structure. Or the members may be nonoligomeric molecules assembled like a jigsaw puzzle, but wherein each piece has both one or more variable moieties (contributing to library diversity) and one or more constant moieties (providing the functionalities for coupling the piece in question to other pieces).

Thus, in a typical combinatorial library, chemical building blocks are at least partially randomly combined into a large number (as high as  $10^{15}$ ) of different compounds, which are then simultaneously screened for binding (or other) activity against one or more targets.

In a "simple combinatorial library", all of the members belong to the same class of compounds (e.g., peptides) and can be synthesized simultaneously. A "composite combinatorial library" is a mixture of two or more simple libraries, e.g., DNAs and peptides, or peptides, peptoids, and PNAs, or benzodiazepines and carbamates. The number of component simple libraries in a composite library will, of course, normally be smaller than the average number of members in each simple library, as otherwise the advantage of a library over individual synthesis is small.

Libraries of thousands, even millions, of random oligopeptides have been prepared by chemical synthesis (Houghten *et al.*, *Nature*, 354:84-6(1991)), or gene expression (Marks *et al.*, *J Mol Biol*, 222:581-97(1991)), displayed on chromatographic supports (Lam *et al.*, *Nature*, 354:82-4(1991)), inside bacterial cells (Colas *et al.*, *Nature*, 380:548-550(1996)), on bacterial pili (Lu, *Bio/Technology*, 13:366-372(1990)), or phage (Smith, *Science*, 228:1315-7(1985)), and screened for binding to a variety of targets including antibodies (Valadon *et al.*, *J Mol Biol*, 261:11-22(1996)), cellular proteins (Schmitz *et al.*, *J Mol Biol*, 260:664-677(1996)), viral proteins (Hong and Boulanger, *Embo J*, 14:4714-4727(1995)), bacterial proteins (Jacobsson and Frykberg, *Biotechniques*, 18:878-885(1995)), nucleic acids (Cheng *et al.*, *Gene*, 171:1-8(1996)), and plastic (Siani *et al.*, *J Chem Inf Comput Sci*, 34:588-593(1994)).

Libraries of proteins (Ladner, *USP* 4,664,989), peptoids (Simon *et al.*, *Proc Natl Acad Sci U S A*, 89:9367-71(1992)), nucleic acids (Ellington and Szostak, *Nature*, 246:818(1990)), carbohydrates, and small organic molecules (Eichler *et al.*, *Med Res Rev*, 15:481-96(1995)) have also been prepared or suggested for drug screening purposes.

The first combinatorial libraries were composed of peptides or proteins, in which all or selected amino acid positions were randomized. Peptides and proteins can exhibit high and specific binding activity, and can act as catalysts. In consequence, they are of great importance in biological systems.

Nucleic acids have also been used in combinatorial libraries. Their great advantage is the ease with which a nucleic acid with appropriate binding activity can be amplified. As a result, combinatorial libraries composed of nucleic acids can be of low redundancy and hence, of high diversity.

There has also been much interest in combinatorial libraries based on small molecules, which are more suited to pharmaceutical use, especially those which, like benzodiazepines, belong to a chemical class which has

already yielded useful pharmacological agents. The techniques of combinatorial chemistry have been recognized as the most efficient means for finding small molecules that act on these targets. At present, small molecule  
5 combinatorial chemistry involves the synthesis of either pooled or discrete molecules that present varying arrays of functionality on a common scaffold. These compounds are grouped in libraries that are then screened against the target of interest either for binding or for inhibition of  
10 biological activity.

The size of a library is the number of molecules in it. The simple diversity of a library is the number of unique structures in it. There is no formal minimum or maximum diversity. If the library has a very low diversity, the  
15 library has little advantage over just synthesizing and screening the members individually. If the library is of very high diversity, it may be inconvenient to handle, at least without automatizing the process. The simple diversity of a library is preferably at least  $10^1$ ,  $10^2$ ,  
20  $10^3$ ,  $10^4$ ,  $10^6$ ,  $10^7$ ,  $10^8$  or  $10^9$ , the higher the better under most circumstances. The simple diversity is usually not more than  $10^{15}$ , and more usually not more than  $10^{10}$ .

The average sampling level is the size divided by the simple diversity. The expected average sampling level must  
25 be high enough to provide a reasonable assurance that, if a given structure were expected, as a consequence of the library design, to be present, that the actual average sampling level will be high enough so that the structure, if satisfying the screening criteria, will yield a positive  
30 result when the library is screened. Thus, the preferred average sampling level is a function of the detection limit, which in turn is a function of the strength of the signal to be screened.

There are more complex measures of diversity than  
35 simple diversity. These attempt to take into account the degree of structural difference between the various unique sequences. These more complex measures are usually used in the context of small organic compound libraries, see below.

The library members may be presented as solutes in solution, or immobilized on some form of support. In the latter case, the support may be living (cell, virus) or nonliving (bead, plate, etc.). The supports may be separable (cells, virus particles, beads) so that binding and nonbinding members can be separated, or nonseparable (plate). In the latter case, the members will normally be placed on addressable positions on the support. The advantage of a soluble library is that there is no carrier moiety that could interfere with the binding of the members to the support. The advantage of an immobilized library is that it is easier to identify the structure of the members which were positive.

When screening a soluble library, or one with a separable support, the target is usually immobilized. When screening a library on a nonseparable support, the target will usually be labeled.

#### Oligonucleotide Libraries

An oligonucleotide library is a combinatorial library, at least some of whose members are single-stranded oligonucleotides having three or more nucleotides connected by phosphodiester or analogous bonds. The oligonucleotides may be linear, cyclic or branched, and may include non-nucleic acid moieties. The nucleotides are not limited to the nucleotides normally found in DNA or RNA. For examples of nucleotides modified to increase nuclease resistance and chemical stability of aptamers, see Chart 1 in Osborne and Ellington, Chem. Rev., 97: 349-70 (1997). For screening of RNA, see Ellington and Szostak, Nature, 346: 818-22 (1990).

There is no formal minimum or maximum size for these oligonucleotides. However, the number of conformations which an oligonucleotide can assume increases exponentially with its length in bases. Hence, a longer oligonucleotide is more likely to be able to fold to adapt itself to a protein surface. On the other hand, while very long molecules can be synthesized and screened, unless they provide a much superior affinity to that of shorter molecules, they are not likely to be found in the selected population, for the

reasons explained by Osborne and Ellington (1997). Hence, the libraries of the present invention are preferably composed of oligonucleotides having a length of 3 to 100 bases, more preferably 15 to 35 bases. The oligonucleotides in a given library may be of the same or of different lengths.

Oligonucleotide libraries have the advantage that libraries of very high diversity (e.g.,  $10^{15}$ ) are feasible, and binding molecules are readily amplified in vitro by polymerase chain reaction (PCR). Moreover, nucleic acid molecules can have very high specificity and affinity to targets.

In a preferred embodiment, this invention prepares and screens oligonucleotide libraries by the SELEX method, as described in King and Famulok, *Molec. Biol. Repts.*, 20: 97-107 (1994); L. Gold, C. Tuerk. *Methods of producing nucleic acid ligands*, US#5595877; Oliphant et al. *Gene* 44:177 (1986).

The term "aptamer" is conferred on those oligonucleotides which bind the target protein. Such aptamers may be used to characterize the target protein, both directly (through identification of the aptamer and the points of contact between the aptamer and the protein) and indirectly (by use of the aptamer as a ligand to modify the chemical reactivity of the protein).

In a classic oligonucleotide, each nucleotide (monomeric unit) is composed of a phosphate group, a sugar moiety, and either a purine or a pyrimidine base. In DNA, the sugar is deoxyribose and in RNA it is ribose. The nucleotides are linked by 5'-3' phosphodiester bonds.

The deoxyribose phosphate backbone of DNA can be modified to increase resistance to nuclease and to increase penetration of cell membranes. Derivatives such as mono- or dithiophosphates, methyl phosphonates, boranophosphates, formacetals, carbamates, siloxanes, and dimethylenethio- -sulfoxideo- and-sulfonyl- linked species are known in the art.

#### Peptide Library

A peptide is composed of a plurality of amino acid residues joined together by peptidyl ( $\text{-NHCO-}$ ) bonds. A biogenic peptide is a peptide in which the residues are all genetically encoded amino acid residues; it is not necessary that the biogenic peptide actually be produced by gene expression.

Amino acids are the basic building blocks with which peptides and proteins are constructed. Amino acids possess both an amino group ( $\text{-NH}_2$ ) and a carboxylic acid group ( $\text{-COOH}$ ). Many amino acids, but not all, have the alpha amino acid structure  $\text{NH}_2\text{-CHR-COOH}$ , where R is hydrogen, or any of a variety of functional groups.

Twenty amino acids are genetically encoded: Alanine, Arginine, Asparagine, Aspartic Acid, Cysteine, Glutamic Acid, Glutamine, Glycine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Proline, Serine, Threonine, Tryptophan, Tyrosine, and Valine. Of these, all save Glycine are optically isomeric, however, only the L-form is found in humans. Nevertheless, the D-forms of these amino acids do have biological significance; D-Phe, for example, is a known analgesic.

Many other amino acids are also known, including: 2-Aminoadipic acid; 3-Aminoadipic acid; beta-Aminopropionic acid; 2-Aminobutyric acid; 4-Aminobutyric acid (Piperidinic acid); 6-Aminocaproic acid; 2-Aminoheptanoic acid; 2-Aminoisobutyric acid, 3-Aminoisobutyric acid; 2-Aminopimelic acid; 2,4-Diaminobutyric acid; Desmosine; 2,2'-Diaminopimelic acid; 2,3-Diaminopropionic acid; N-Ethylglycine; N-Ethylasparagine; Hydroxylysine; allo-Hydroxylysine; 3-Hydroxyproline; 4-Hydroxyproline; Isodesmosine; allo-Isoleucine; N-Methylglycine (Sarcosine); N-Methylisoleucine; N-Methylvaline; Norvaline; Norleucine; and Ornithine.

Peptides are constructed by condensation of amino acids and/or smaller peptides. The amino group of one amino acid (or peptide) reacts with the carboxylic acid group of a second amino acid (or peptide) to form a peptide ( $\text{-NHCO-}$ ) bond, releasing one molecule of water. Therefore, when an amino acid is incorporated into a peptide, it should,



technically speaking, be referred to as an amino acid residue. The core of that residue is the moiety which excludes the -NH and -CO linking functionalities which connect it to other residues. This moiety consists of one or more main chain atoms (see below) and the attached side chains.

The main chain moiety of each amino acid consists of the -NH and -CO linking functionalities and a core main chain moiety. Usually the latter is a single carbon atom. However, the core main chain moiety may include additional carbon atoms, and may also include nitrogen, oxygen or sulfur atoms, which together form a single chain. In a preferred embodiment, the core main chain atoms consist solely of carbon atoms.

The side chains are attached to the core main chain atoms. For alpha amino acids, in which the side chain is attached to the alpha carbon, the C-1, C-2 and N-2 of each residue form the repeating unit of the main chain, and the word "side chain" refers to the C-3 and higher numbered carbon atoms and their substituents. It also includes H atoms attached to the main chain atoms.

Amino acids may be classified according to the number of carbon atoms which appear in the main chain between the carbonyl carbon and amino nitrogen atoms which participate in the peptide bonds. Among the 150 or so amino acids which occur in nature, alpha, beta, gamma and delta amino acids are known. These have 1-4 intermediary carbons. Only alpha amino acids occur in proteins. Proline is a special case of an alpha amino acid; its side chain also binds to the peptide bond nitrogen.

For beta and higher order amino acids, there is a choice as to which main chain core carbon a side chain other than H is attached to. The preferred attachment site is the C-2 (alpha) carbon, i.e., the one adjacent to the carboxyl carbon of the -CO linking functionality. It is also possible for more than one main chain atom to carry a side chain other than H. However, in a preferred embodiment, only one main chain core atom carries a side chain other than H.

A main chain carbon atom may carry either one or two side chains; one is more common. A side chain may be attached to a main chain carbon atom by a single or a double bond; the former is more common.

5       A simple combinatorial peptide library is one whose members are peptides having three or more amino acids connected via peptide bonds.

      The peptides may be linear, branched, or cyclic, and may covalently or noncovalently include nonpeptidyl  
10       moieties. The amino acids are not limited to the naturally occurring or to the genetically encoded amino acids.

      A biased peptide library is one in which one or more (but not all) residues of the peptides are constant residues.

15

### *Cyclic Peptides*

      Many naturally occurring peptides are cyclic. Cyclization is a common mechanism for stabilization of peptide conformation thereby achieving improved association  
20       of the peptide with its ligand and hence improved biological activity. Cyclization is usually achieved by intra-chain cystine formation, by formation of peptide bond between side chains or between N- and C- terminals. Cyclization was usually achieved by peptides in solution, but several  
25       publications have appeared that describe cyclization of peptides on beads.

      A peptide library may be an oligopeptide library or a protein library.

### 30       *Oligopeptides*

      Preferably, the oligopeptides are at least five, six, seven or eight amino acids in length. Preferably, they are composed of less than 50, more preferably less than 20 amino acids.

35       In the case of an oligopeptide library, all or just some of the residues may be variable. The oligopeptide may be unconstrained, or constrained to a particular conformation by, e.g., the participation of constant

cysteine residues in the formation of a constraining disulfide bond.

### *Proteins*

5       Proteins, like oligopeptides, are composed of a plurality of amino acids, but the term protein is usually reserved for longer peptides, which are able to fold into a stable conformation. A protein may be composed of two or more polypeptide chains, held together by covalent or  
10       noncovalent crosslinks. These may occur in a homooligomeric or a heterooligomeric state.

      A peptide is considered a protein if it (1) is at least 50 amino acids long, or (2) has at least two stabilizing covalent crosslinks (e.g., disulfide bonds). Thus,  
15       conotoxins are considered proteins.

      Usually, the proteins of a protein library will be characterizable as having both constant residues (the same for all proteins in the library) and variable residues (which vary from member to member). This is simply because,  
20       for a given range of variation at each position, the sequence space (simple diversity) grows exponentially with the number of residue positions, so at some point it becomes inconvenient for all residues of a peptide to be variable positions. Since proteins are usually larger than  
25       oligopeptides, it is more common for protein libraries than oligopeptide libraries to feature variable positions.

      In the case of a protein library, it is desirable to focus the mutations at those sites which are tolerant of mutation. These may be determined by alanine scanning  
30       mutagenesis or by comparison of the protein sequence to that of homologous proteins of similar activity. It is also more likely that mutation of surface residues will directly affect binding. Surface residues may be determined by inspecting a 3D structure of the protein, or by labeling the  
35       surface and then ascertaining which residues have received labels. They may also be inferred by identifying regions of high hydrophilicity within the protein.

Because proteins are often altered at some sites but not others, protein libraries can be considered a special case of the biased peptide library.

There are several reasons that one might screen a protein library instead of an oligopeptide library, including (1) a particular protein, mutated in the library, has the desired activity to some degree already, and (2) the oligopeptides are not expected to have a sufficiently high affinity or specificity since they do not have a stable conformation.

When the protein library is based on a parental protein which does not have the desired activity, the parental protein will usually be one which is of high stability (melting point  $\geq 50$  deg. C.) and/or possessed of hypervariable regions.

The variable domains of an antibody possess hypervariable regions and hence, in some embodiments, the protein library comprises members which comprise a mutant of VH or VL chain, or a mutant of an antigen-specific binding fragment of such a chain. VH and VL chains are usually each about 110 amino acid residues, and are held in proximity by a disulfide bond between the adjoining CL and CH1 regions to form a variable domain. Together, the VH, VL, CL and CH1 form an Fab fragment.

In human heavy chains, the hypervariable regions are at 31-35, 49-65, 98-111 and 84-88, but only the first three are involved in antigen binding. There is variation among VH and VL chains at residues outside the hypervariable regions, but to a much lesser degree.

A sequence is considered a mutant of a VH or VL chain if it is at least 80% identical to a naturally occurring VH or VL chain at all residues outside the hypervariable region.

In a preferred embodiment, such antibody library members comprise both at least one VH chain and at least one VL chain, at least one of which is a mutant chain, and which chains may be derived from the same or different antibodies. The VH and VL chains may be covalently joined by a suitable linker moiety, as in a "single chain antibody", or they may

be noncovalently joined, as in a naturally occurring variable domain.

If the joining is noncovalent, and the library is displayed on cells or virus, then either the VH or the VL chain may be fused to the carrier surface/coat protein. The complementary chain may be co-expressed, or added exogenously to the library.

The members may further comprise some or all of an antibody constant heavy and/or constant light chain, or a mutant thereof.

### Peptoid Library

A peptoid is an analogue of a peptide in which one or more of the peptide bonds (-NH-CO-) are replaced by pseudopeptide bonds, which may be the same or different. It is not necessary that all of the peptide bonds be replaced, i.e., a peptoid may include one or more conventional amino acid residues, e.g., proline.

A peptide bond has two small divalent linker elements, -NH- and -CO-. Thus, a preferred class of pseudopeptide bonds are those which consist of two small divalent linker elements. Each may be chosen independently from the group consisting of amine (-NH-), substituted amine (-NR-), carbonyl (-CO-), thiocarbonyl (-CS-), methylene (-CH<sub>2</sub>-), monosubstituted methylene (-CHR-), disubstituted methylene (-CR<sub>1</sub>R<sub>2</sub>-), ether (-O-) and thioether (-S-). The more preferred pseudopeptide bonds include:

N-modified -NRCO-

Carba  $\Psi$  -CH<sub>2</sub>-CH<sub>2</sub>-

Depsi  $\Psi$  -CO-O-

Hydroxyethylene  $\Psi$  -CHOH-CH<sub>2</sub>-

Ketomethylene  $\Psi$  -CO-CH<sub>2</sub>-

Methylene-Oxy -CH<sub>2</sub>-O-

Reduced -CH<sub>2</sub>-NH-

Thiomethylene -CH<sub>2</sub>-S-

Thiopeptide -CS-NH-

Retro-Inverso -CO-NH-

A single peptoid molecule may include more than one kind of pseudopeptide bond.

For the purposes of introducing diversity into a peptoid library, one may vary (1) the side chains attached to the core main chain atoms of the monomers linked by the pseudopeptide bonds, and/or (2) the side chains (e.g., the R of an -NRCO-) of the pseudopeptide bonds. Thus, in one embodiment, the monomeric units which are not amino acid residues are of the structure -NR<sub>1</sub>-CR<sub>2</sub>-CO-, where at least one of R<sub>1</sub> and R<sub>2</sub> are not hydrogen. If there is variability in the pseudopeptide bond, this is most conveniently done by using an -NRCO- or other pseudopeptide bond with an R group, and varying the R group. In this event, the R group will usually be any of the side chains characterizing the amino acids of peptides, as previously discussed.

If the R group of the pseudopeptide bond is not variable, it will usually be small, e.g., not more than 10 atoms (e.g., hydroxyl, amino, carboxyl, methyl, ethyl, propyl).

If the conjugation chemistries are compatible, a simple combinatorial library may include both peptides and peptoids.

#### Peptide Nucleic Acid Library

A PNA oligomer is here defined as one comprising a plurality of units, at least one of which is a PNA monomer which comprises a side chain comprising a nucleobase. For nucleobases, see USP 6,077,835.

The classic PNA oligomer is composed of (2-aminoethyl)glycine units, with nucleobases attached by methylene carbonyl linkers. That is, it has the structure



where the outer parenthesized substructure is the PNA monomer.

In this structure, the nucleobase B is separated from the backbone N by three bonds, and the points of attachment

of the side chains are separated by six bonds. The nucleobase may be any of the bases included in the nucleotides discussed in connection with oligonucleotide libraries. The bases of nucleotides A, G, T, C and U are preferred.

A PNA oligomer may further comprise one or more amino acid residues, especially glycine and proline.

One can readily envision related molecules in which (1) the -COCH<sub>2</sub>- linker is replaced by another linker, especially one composed of two small divalent linkers as defined previously, (2) a side chain is attached to one of the three main chain carbons not participating in the peptide bond (either instead or in addition to the side chain attached to the N of the classic PNA); and/or (3) the peptide bonds are replaced by pseudopeptide bonds as disclosed previously in the context of peptoids.

PNA oligomer libraries have been made; see e.g. Cook, 6,204,326.

#### Small Organic Compound Library

The small organic compound library ("compound library", for short) is a combinatorial library whose members are suitable for use as drugs if, indeed, they have the ability to mediate a biological activity of the target protein.

Peptides have certain disadvantages as drugs. These include susceptibility to degradation by serum proteases, and difficulty in penetrating cell membranes. Preferably, all or most of the compounds of the compound library avoid, or at least do not suffer to the same degree, one or more of the pharmaceutical disadvantages of peptides.

In designing a compound library, it is helpful to bear in mind the methods of molecular modification typically used to obtain new drugs. Three basic kinds of modification may be identified: disjunction, in which a lead drug is simplified to identify its component pharmacophoric moieties; conjunction, in which two or more known pharmacophoric moieties, which may be the same or different, are associated, covalently or noncovalently, to form a new drug; and alteration, in which one moiety is replaced by

another which may be similar or different, but which is not in effect a disjunction or conjunction. The use of the terms "disjunction", "conjunction" and "alteration" is intended only to connote the structural relationship of the end product to the original leads, and not how the new drugs are actually synthesized, although it is possible that the two are the same.

The process of disjunction is illustrated by the evolution of neostigmine (1931) and edrophonium (1952) from physostigmine (1925). Subsequent conjunction is illustrated by demecarium (1956) and ambenonium (1956).

Alterations may modify the size, polarity, or electron distribution of an original moiety. Alterations include ring closing or opening, formation of lower or higher homologues, introduction or saturation of double bonds, introduction of optically active centers, introduction, removal or replacement of bulky groups, isosteric or bioisosteric substitution, changes in the position or orientation of a group, introduction of alkylating groups, and introduction, removal or replacement of groups with a view toward inhibiting or promoting inductive (electrostatic) or conjugative (resonance) effects.

Thus, the substituents may include electron acceptors and/or electron donors. Typical electron donors (+I) include  $-\text{CH}_3$ ,  $-\text{CH}_2\text{R}$ ,  $-\text{CHR}_2$ ,  $-\text{CR}_3$  and  $-\text{COO}^-$ . Typical electron acceptors (-I) include  $-\text{NH}_3^+$ ,  $-\text{NR}_3^+$ ,  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{COOH}$ ,  $-\text{COOR}$ ,  $-\text{CHO}$ ,  $-\text{COR}$ ,  $-\text{COR}$ ,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{OH}$ ,  $-\text{OR}$ ,  $-\text{SH}$ ,  $-\text{SR}$ ,  $-\text{CH}=\text{CH}_2$ ,  $-\text{CR}=\text{CR}_2$ , and  $-\text{C}=\text{CH}$ .

The substituents may also include those which increase or decrease electronic density in conjugated systems. The former (+R) groups include  $-\text{CH}_3$ ,  $-\text{CR}_3$ ,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{OR}$ ,  $-\text{OCOR}$ ,  $-\text{SH}$ ,  $-\text{SR}$ ,  $-\text{NH}_2$ ,  $-\text{NR}_2$ , and  $-\text{NHCOR}$ . The later (-R) groups include  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{CHC}$ ,  $-\text{COR}$ ,  $-\text{COOH}$ ,  $-\text{COOR}$ ,  $-\text{CONH}_2$ ,  $-\text{SO}_2\text{R}$  and  $-\text{CF}_3$ .

Synthetically speaking, the modifications may be achieved by a variety of unit processes, including nucleophilic and electrophilic substitution, reduction and oxidation, addition elimination, double bond cleavage, and cyclization.



For the purpose of constructing a library, a compound, or a family of compounds, having one or more pharmacological activities (which need not be related to the known or suspected activities of the target protein), may be disjoined into two or more known or potential pharmacophoric moieties. Analogues of each of these moieties may be identified, and mixtures of these analogues reacted so as to reassemble compounds which have some similarity to the original lead compound. It is not necessary that all members of the library possess moieties analogous to all of the moieties of the lead compound.

The design of a library may be illustrated by the example of the benzodiazepines. Several benzodiazepine drugs, including chlordiazepoxide, diazepam and oxazepam, have been used as anti-anxiety drugs. Derivatives of benzodiazepines have widespread biological activities; derivatives have been reported to act not only as anxiolytics, but also as anticonvulsants; cholecystokinin (CCK) receptor subtype A or B, kappa opioid receptor, platelet activating factor, and HIV transactivator Tat antagonists, and GPIIbIIIa, reverse transcriptase and ras farnesyltransferase inhibitors.

The benzodiazepine structure has been disjoined into a 2-aminobenzophenone, an amino acid, and an alkylating agent. See Bunin, et al., Proc. Nat. Acad. Sci. USA, 91:4708 (1994). Since only a few 2-aminobenzophenone derivatives are commercially available, it was later disjoined into 2-aminoarylstannane, an acid chloride, an amino acid, and an alkylating agent. Bunin, et al., Meth. Enzymol., 267:448 (1996). The arylstannane may be considered the core structure upon which the other moieties are substituted, or all four may be considered equals which are conjoined to make each library member.

A basic library synthesis plan and member structure is shown in Figure 1 of Fowlkes, et al., U.S. Serial No. 08/740,671, incorporated by reference in its entirety. The acid chloride building block introduces variability at the R<sup>1</sup> site. The R<sup>2</sup> site is introduced by the amino acid, and the R<sup>3</sup> site by the alkylating agent. The R<sup>4</sup> site is inherent in

the arylstannane. Bunin, et al. generated a 1, 4-benzodiazepine library of 11,200 different derivatives prepared from 20 acid chlorides, 35 amino acids, and 16 alkylating agents. (No diversity was introduced at R<sup>4</sup>; this group was used to couple the molecule to a solid phase.) According to the Available Chemicals Directory (HDL Information Systems, San Leandro CA), over 300 acid chlorides, 80 Fmoc-protected amino acids and 800 alkylating agents were available for purchase (and more, of course, could be synthesized). The particular moieties used were chosen to maximize structural dispersion, while limiting the numbers to those conveniently synthesized in the wells of a microtiter plate. In choosing between structurally similar compounds, preference was given to the least substituted compound.

The variable elements included both aliphatic and aromatic groups. Among the aliphatic groups, both acyclic and cyclic (mono- or poly-) structures, substituted or not, were tested. (While all of the acyclic groups were linear, it would have been feasible to introduce a branched aliphatic). The aromatic groups featured either single and multiple rings, fused or not, substituted or not, and with heteroatoms or not. The secondary substituents included -NH<sub>2</sub>, -OH, -OMe, -CN, -Cl, -F, and -COOH. While not used, spacer moieties, such as -O-, -S-, -OO-, -CS-, -NH-, and -NR-, could have been incorporated.

Bunin et al. suggest that instead of using a 1, 4-benzodiazepine as a core structure, one may instead use a 1, 4-benzodiazepine-2, 5-dione structure.

As noted by Bunin et al., it is advantageous, although not necessary, to use a linkage strategy which leaves no trace of the linking functionality, as this permits construction of a more diverse library.

Other combinatorial nonoligomeric compound libraries known or suggested in the art have been based on carbamates, mercaptoacylated pyrrolidines, phenolic agents, aminimides, N-acylamino ethers (made from amino alcohols, aromatic hydroxy acids, and carboxylic acids), N-alkylamino ethers

(made from aromatic hydroxy acids, amino alcohols and aldehydes) 1, 4-piperazines, and 1, 4-piperazine-6-ones.

DeWitt, et al., Proc. Nat. Acad. Sci. (USA), 90:6909-13 (1993) describe the simultaneous but separate, synthesis of 40 discrete hydantoins and 40 discrete benzodiazepines. They carry out their synthesis on a solid support (inside a gas dispersion tube), in an array format, as opposed to other conventional simultaneous synthesis techniques (e.g., in a well, or on a pin). The hydantoins were synthesized by first simultaneously deprotecting and then treating each of five amino acid resins with each of eight isocyanates. The benzodiazepines were synthesized by treating each of five deprotected amino acid resins with each of eight 2-amino benzophenone imines.

Chen, et al., J. Am. Chem. Soc., 116:2661-62 (1994) described the preparation of a pilot (9 member) combinatorial library of formate esters. A polymer bead-bound aldehyde preparation was "split" into three aliquots, each reacted with one of three different ylide reagents. The reaction products were combined, and then divided into three new aliquots, each of which was reacted with a different Michael donor. Compound identity was found to be determinable on a single bead basis by gas chromatography/mass spectroscopy analysis.

Holmes, USP 5,549,974 (1996) sets forth methodologies for the combinatorial synthesis of libraries of thiazolidinones and metathiazanones. These libraries are made by combination of amines, carbonyl compounds, and thiols under cyclization conditions.

Ellman, USP 5,545,568 (1996) describes combinatorial synthesis of benzodiazepines, prostaglandins, beta-turn mimetics, and glycerol-based compounds. See also Ellman, USP 5,288,514.

Summerton, USP 5,506,337 (1996) discloses methods of preparing a combinatorial library formed predominantly of morpholino subunit structures.

Heterocyclic combinatorial libraries are reviewed generally in Nefzi, et al., Chem. Rev., 97:449-472 (1997).

For pharmacological classes, see, e.g., Goth, Medical Pharmacology: Principles and Concepts (C.V. Mosby Co.: 8th ed. 1976); Korolkovas and Burckhalter, Essentials of Medicinal Chemistry (John Wiley & Sons, Inc.: 1976). For  
5 synthetic methods, see, e.g., Warren, Organic Synthesis: The Disconnection Approach (John Wiley & Sons, Ltd.: 1982); Fuson, Reactions of Organic Compounds (John Wiley & Sons: 1966); Payne and Payne, How to do an Organic Synthesis (Allyn and Bacon, Inc.: 1969); Greene, Protective Groups in  
10 Organic Synthesis (Wiley-Interscience). For selection of substituents, see e.g., Hansch and Leo, Substituent Constants for Correlation Analysis in Chemistry and Biology (John Wiley & Sons: 1979).

The library is preferably synthesized so that the  
15 individual members remain identifiable so that, if a member is shown to be active, it is not necessary to analyze it. Several methods of identification have been proposed, including:

(1) encoding, i.e., the attachment to each member of  
20 an identifier moiety which is more readily identified than the member proper. This has the disadvantage that the tag may itself influence the activity of the conjugate.

(2) spatial addressing, e.g., each member is  
25 synthesized only at a particular coordinate on or in a matrix, or in a particular chamber. This might be, for example, the location of a particular pin, or a particular well on a microtiter plate, or inside a "tea bag".

30 The present invention is not limited to any particular form of identification.

However, it is possible to simply characterize those  
members of the library which are found to be active, based  
on the characteristic spectroscopic indicia of the various  
35 building blocks.

Solid phase synthesis permits greater control over  
which derivatives are formed. However, the solid phase  
could interfere with activity. To overcome this problem,

some or all of the molecules of each member could be liberated, after synthesis but before screening.

Examples of candidate simple libraries which might be evaluated include derivatives of the following:

- 5       Cyclic Compounds Containing One Hetero Atom
  - Heteronitrogen
    - pyrroles
      - pentasubstituted pyrroles
    - pyrrolidines
    - 10       pyrrolines
    - prolines
    - indoles
    - beta-carbolines
    - pyridines
    - 15       dihydropyridines
      - 1,4-dihydropyridines
      - pyrido[2,3-d]pyrimidines
      - tetrahydro-3H-imidazo[4,5-c] pyridines
    - Isoquinolines
    - 20       tetrahydroisoquinolines
    - quinolones
    - beta-lactams
      - azabicyclo[4.3.0]nonen-8-one amino acid
  - Heterooxygen
    - 25       furans
      - tetrahydrofurans
        - 2,5-disubstituted tetrahydrofurans
    - pyrans
      - hydroxypyranones
      - 30       tetrahydroxypyranones
    - gamma-butyrolactones
  - Heterosulfur
    - sulfolenes
- 35       Cyclic Compounds with Two or More Hetero atoms
  - Multiple heteronitrogens
    - imidazoles
    - pyrazoles
    - piperazines
      - diketopiperazines

	arylpiperazines	
	benzylpiperazines	
	benzodiazepines	
	1,4-benzodiazepine-2,5-diones	
5	hydantoins	
	5-alkoxyhydantoins	
	dihydropyrimidines	
	1,3-disubstituted-5,6-dihydropyrimidine-2,4-	
10	diones	
	cyclic ureas	
	cyclic thioureas	
	quinazolines	
	chiral 3-substituted-quinazoline-2,4-	
15	diones	
	triazoles	
	1,2,3-triazoles	
	purines	
	Heteronitrogen and Heterooxygen	
20	dikelomorpholines	
	isoxazoles	
	isoxazolines	
	Heteronitrogen and Heterosulfur	
	thiazolidines	
25	N-axylthiazolidines	
	dihydrothiazoles	
	2-methylene-2,3-dihydrothiazates	
	2-aminothiazoles	
	thiophenes	
30	3-amino thiophenes	
	4-thiazolidinones	
	4-melathiazanones	
	benzisothiazolones	

35 For details on synthesis of libraries, see Nefzi, et al., Chem. Rev., 97:449-72 (1997), and references cited therein.

#### Pharmaceutical Methods and Preparations

The preferred animal subject of the present invention is a mammal. By the term "mammal" is meant an individual belonging to the class Mammalia. The invention is particularly useful in the treatment of human subjects, although it is intended for veterinary and nutritional uses as well. Preferred nonhuman subjects are of the orders Primata (e.g., apes and monkeys), Artiodactyla or Perissodactyla (e.g., cows, pigs, sheep, horses, goats), Carnivora (e.g., cats, dogs), Rodenta (e.g., rats, mice, guinea pigs, hamsters), Lagomorpha (e.g., rabbits) or other pet, farm or laboratory mammals.

The term "protection", as used herein, is intended to include "prevention," "suppression" and "treatment." "Prevention", strictly speaking, involves administration of the pharmaceutical prior to the induction of the disease (or other adverse clinical condition). "Suppression" involves administration of the composition prior to the clinical appearance of the disease. "Treatment" involves administration of the protective composition after the appearance of the disease.

It will be understood that in human and veterinary medicine, it is not always possible to distinguish between "preventing" and "suppressing" since the ultimate inductive event or events may be unknown, latent, or the patient is not ascertained until well after the occurrence of the event or events. Therefore, unless qualified, the term "prevention" will be understood to refer to both prevention in the strict sense, and to suppression.

The preventative or prophylactic use of a pharmaceutical usually involves identifying subjects who are at higher risk than the general population of contracting the disease, and administering the pharmaceutical to them in advance of the clinical appearance of the disease. The effectiveness of such use is measured by comparing the subsequent incidence or severity of the disease, or of particular symptoms of the disease, in the treated subjects against that in untreated subjects of the same high risk group.

While high risk factors vary from disease to disease, in general, these include (1) prior occurrence of the disease in one or more members of the same family, or, in the case of a contagious disease, in individuals with whom the subject has come into potentially contagious contact at a time when the earlier victim was likely to be contagious, (2) a prior occurrence of the disease in the subject, (3) prior occurrence of a related disease, or a condition known to increase the likelihood of the disease, in the subject; (4) appearance of a suspicious level of a marker of the disease, or a related disease or condition; (5) a subject who is immunologically compromised, e.g., by radiation treatment, HIV infection, drug use,, etc., or (6) membership in a particular group (e.g., a particular age, sex, race, ethnic group, etc.) which has been epidemiologically associated with that disease.

In some cases, it may be desirable to provide prophylaxis for the general population, and not just a high risk group. This is most likely to be the case when essentially all are at risk of contracting the disease, the effects of the disease are serious, the therapeutic index of the prophylactic agent is high, and the cost of the agent is low.

A prophylaxis or treatment may be curative, that is, directed at the underlying cause of a disease, or ameliorative, that is, directed at the symptoms of the disease, especially those which reduce the quality of life.

It should also be understood that to be useful, the protection provided need not be absolute, provided that it is sufficient to carry clinical value. An agent which provides protection to a lesser degree than do competitive agents may still be of value if the other agents are ineffective for a particular individual, if it can be used in combination with other agents to enhance the level of protection, or if it is safer than competitive agents. It is desirable that there be a statistically significant ( $p=0.05$  or less) improvement in the treated subject relative to an appropriate untreated control, and it is desirable that this improvement be at least 10%, more preferably at least 25%,



still more preferably at least 50%, even more preferably at least 100%, in some indicia of the incidence or severity of the disease or of at least one symptom of the disease.

At least one of the drugs of the present invention may be administered, by any means that achieve their intended purpose, to protect a subject against a disease or other adverse condition. The form of administration may be systemic or topical. For example, administration of such a composition may be by various parenteral routes such as subcutaneous, intravenous, intradermal, intramuscular, intraperitoneal, intranasal, transdermal, or buccal routes. Alternatively, or concurrently, administration may be by the oral route. Parenteral administration can be by bolus injection or by gradual perfusion over time.

A typical regimen comprises administration of an effective amount of the drug, administered over a period ranging from a single dose, to dosing over a period of hours, days, weeks, months, or years.

It is understood that the suitable dosage of a drug of the present invention will be dependent upon the age, sex, health, and weight of the recipient, kind of concurrent treatment, if any, frequency of treatment, and the nature of the effect desired. However, the most preferred dosage can be tailored to the individual subject, as is understood and determinable by one of skill in the art, without undue experimentation. This will typically involve adjustment of a standard dose, e.g., reduction of the dose if the patient has a low body weight.

Prior to use in humans, a drug will first be evaluated for safety and efficacy in laboratory animals. In human clinical studies, one would begin with a dose expected to be safe in humans, based on the preclinical data for the drug in question, and on customary doses for analogous drugs (if any). If this dose is effective, the dosage may be decreased, to determine the minimum effective dose, if desired. If this dose is ineffective, it will be cautiously increased, with the patients monitored for signs of side effects. See, e.g., Berkow et al, eds., *The Merck Manual*, 15th edition, Merck and Co., Rahway, N.J., 1987; Goodman et

al., eds., *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 8th edition, Pergamon Press, Inc., Elmsford, N.Y., (1990); *Avery's Drug Treatment: Principles and Practice of Clinical Pharmacology and Therapeutics*, 3rd edition, ADIS Press, LTD., Williams and Wilkins, Baltimore, MD. (1987), Ebadi, *Pharmacology*, Little, Brown and Co., Boston, (1985), which references and references cited therein, are entirely incorporated herein by reference.

The total dose required for each treatment may be administered by multiple doses or in a single dose. The protein may be administered alone or in conjunction with other therapeutics directed to the disease or directed to other symptoms thereof.

Typical pharmaceutical doses, for adult humans, are in the range of 1 ng to 10g per day, more often 1 mg to 1g per day.

The appropriate dosage form will depend on the disease, the pharmaceutical, and the mode of administration; possibilities include tablets, capsules, lozenges, dental pastes, suppositories, inhalants, solutions, ointments and parenteral depots. See, e.g., Berker, *supra*, Goodman, *supra*, Avery, *supra* and Ebadi, *supra*, which are entirely incorporated herein by reference, including all references cited therein.

In the case of peptide drugs, the drug may be administered in the form of an expression vector comprising a nucleic acid encoding the peptide; such a vector, after incorporation into the genetic complement of a cell of the patient, directs synthesis of the peptide. Suitable vectors include genetically engineered poxviruses (vaccinia), adenoviruses, adeno-associated viruses, herpesviruses and lentiviruses which are or have been rendered nonpathogenic.

In addition to at least one drug as described herein, a pharmaceutical composition may contain suitable pharmaceutically acceptable carriers, such as excipients, carriers and/or auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. See, e.g., Berker, *supra*, Goodman, *supra*, Avery, *supra* and Ebadi, *supra*, which are entirely

incorporated herein by reference, included all references cited therein.

### **Assay Compositions and Methods**

#### 5     Target Organism

The invention contemplates that it may be appropriate to ascertain or to mediate the biological activity of a substance of this invention in a target organism.

10     The target organism may be a plant, animal, or microorganism.

In the case of a plant, it may be an economic plant, in which case the drug may be intended to increase the disease, weather or pest resistance, alter the growth characteristics, or otherwise improve the useful  
15     characteristics or mute undesirable characteristics of the plant. Or it may be a weed, in which case the drug may be intended to kill or otherwise inhibit the growth of the plant, or to alter its characteristics to convert it from a weed to an economic plant. The plant may be a tree, shrub,  
20     crop, grass, etc. The plant may be an algae (which are in some cases also microorganisms), or a vascular plant, especially gymnosperms (particularly conifers) and angiosperms. Angiosperms may be monocots or dicots. The plants of greatest interest are rice, wheat, corn, alfalfa,  
25     soybeans, potatoes, peanuts, tomatoes, melons, apples, pears, plums, pineapples, fir, spruce, pine, cedar, and oak.

If the target organism is a microorganism, it may be algae, bacteria, fungi, or a virus (although the biological  
30     activity of a virus must be determined in a virus-infected cell). The microorganism may be human or other animal or plant pathogen, or it may be nonpathogenic. It may be a soil or water organism, or one which normally lives inside other living things.

If the target organism is an animal, it may be a  
35     vertebrate or a nonvertebrate animal. Nonvertebrate animals are chiefly of interest when they act as pathogens or parasites, and the drugs are intended to act as biocidal or biostatic agents. Nonvertebrate animals of interest include worms, mollusks, and arthropods.

The target organism may also be a vertebrate animal, i.e., a mammal, bird, reptile, fish or amphibian. Among mammals, the target animal preferably belongs to the order Primata (humans, apes and monkeys), Artiodactyla (e.g., cows, pigs, sheep, goats, horses), Rodenta (e.g., mice, rats) Lagomorpha (e.g., rabbits, hares), or Carnivora (e.g., cats, dogs). Among birds, the target animals are preferably of the orders Anseriformes (e.g., ducks, geese, swans) or Galliformes (e.g., quails, grouse, pheasants, turkeys and chickens). Among fish, the target animal is preferably of the order Clupeiformes (e.g., sardines, shad, anchovies, whitefish, salmon).

### Target Tissues

The term "target tissue" refers to any whole animal, physiological system, whole organ, part of organ, miscellaneous tissue, cell, or cell component (e.g., the cell membrane) of a target animal in which biological activity may be measured.

Routinely in mammals one would choose to compare and contrast the biological impact on virtually any and all tissues which express the subject receptor protein. The main tissues to use are: brain, heart, lung, kidney, liver, pancreas, skin, intestines, adipose, stomach, skeletal muscle, adrenal glands, breast, prostate, vasculature, retina, cornea, thyroid gland, parathyroid glands, thymus, bone marrow, bone, etc.

Another classification would be by cell type: B cells, T cells, macrophages, neutrophils, eosinophils, mast cells, platelets, megakaryocytes, erythrocytes, bone marrow stromal cells, fibroblasts, neurons, astrocytes, neuroglia, microglia, epithelial cells (from any organ, e.g. skin, breast, prostate, lung, intestines etc), cardiac muscle cells, smooth muscle cells, striated muscle cells, osteoblasts, osteocytes, chondroblasts, chondrocytes, keratinocytes, melanocytes, etc.

Of course, in the case of a unicellular organism, there is no distinction between the "target organism" and the "target tissue".

### Screening Assays

Assays intended to determine the binding or the biological activity of a substance are called preliminary screening assays.

Screening assays will typically be either *in vitro* (cell-free) assays (for binding to an immobilized receptor) or cell-based assays (for alterations in the phenotype of the cell). They will not involve screening of whole multicellular organisms, or isolated organs. The comments on diagnostic biological assays apply mutatis mutandis to screening cell-based assays.

### In Vitro vs. In Vivo Assays

The term *in vivo* is descriptive of an event, such as binding or enzymatic action, which occurs within a living organism. The organism in question may, however, be genetically modified. The term *in vitro* refers to an event which occurs outside a living organism. Parts of an organism (e.g., a membrane, or an isolated biochemical) are used, together with artificial substrates and/or conditions. For the purpose of the present invention, the term *in vitro* excludes events occurring inside or on an intact cell, whether of a unicellular or multicellular organism.

*In vivo* assays include both cell-based assays, and organismic assays. The cell-based assays include both assays on unicellular organisms, and assays on isolated cells or cell cultures derived from multicellular organisms. The cell cultures may be mixed, provided that they are not organized into tissues or organs. The term organismic assay refers to assays on whole multicellular organisms, and assays on isolated organs or tissues of such organisms.

### In vitro Diagnostic Methods and Reagents

The *in vitro* assays of the present invention may be applied to any suitable analyte-containing sample, and may be qualitative or quantitative in nature.

### *Sample*

The sample will normally be a biological fluid, such as blood, urine, lymph, semen, milk, or cerebrospinal fluid, or a fraction or derivative thereof, or a biological tissue, in the form of, e.g., a tissue section or homogenate. However, the sample conceivably could be (or derived from) a food or beverage, a pharmaceutical or diagnostic composition, soil, or surface or ground water. If a biological fluid or tissue, it may be taken from a human or other mammal, vertebrate or animal, or from a plant. The preferred sample is blood; or a fraction or derivative thereof.

### *Binding and Reaction Assays*

The assay may be a binding assay, in which one step involves the binding of a diagnostic reagent to the analyte, or a reaction assay, which involves the reaction of a reagent with the analyte. The reagents used in a binding assay may be classified as to the nature of their interaction with analyte: (1) analyte analogues, or (2) analyte binding molecules (ABM). They may be labeled or insolubilized.

In a reaction assay, the assay may look for a direct reaction between the analyte and a reagent which is reactive with the analyte, or if the analyte is an enzyme or enzyme inhibitor, for a reaction catalyzed or inhibited by the analyte. The reagent may be a reactant, a catalyst, or an inhibitor for the reaction.

An assay may involve a cascade of steps in which the product of one step acts as the target for the next step. These steps may be binding steps, reaction steps, or a combination thereof.

### *Signal Producing System (SPS)*

In order to detect the presence, or measure the amount, of an analyte, the assay must provide for a signal producing system (SPS) in which there is a detectable difference in the signal produced, depending on whether the analyte is present or absent (or, in a quantitative assay, on the

amount of the analyte). The detectable signal may be one which is visually detectable, or one detectable only with instruments. Possible signals include production of colored or luminescent products, alteration of the characteristics (including amplitude or polarization) of absorption or emission of radiation by an assay component or product, and precipitation or agglutination of a component or product. The term "signal" is intended to include the discontinuance of an existing signal, or a change in the rate of change of an observable parameter, rather than a change in its absolute value. The signal may be monitored manually or automatically.

In a reaction assay, the signal is often a product of the reaction. In a binding assay, it is normally provided by a label borne by a labeled reagent.

### *Labels*

The component of the signal producing system which is most intimately associated with the diagnostic reagent is called the "label". A label may be, e.g., a radioisotope, a fluorophore, an enzyme, a co-enzyme, an enzyme substrate, an electron-dense compound, an agglutinable particle.

The radioactive isotope can be detected by such means as the use of a gamma counter or a scintillation counter or by autoradiography. Isotopes which are particularly useful for the purpose of the present invention include  $^3\text{H}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$ ,  $^{14}\text{C}$ ,  $^{32}\text{P}$  and  $^{33}\text{P}$ .  $^{125}\text{I}$  is preferred for antibody labeling.

The label may also be a fluorophore. When the fluorescently labeled reagent is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, o-phthaldehyde and fluorescamine.

Alternatively, fluorescence-emitting metals such as  $^{125}\text{Eu}$ , or others of the lanthanide series, may be incorporated into a diagnostic reagent using such metal

chelating groups as diethylenetriaminepentaacetic acid (DTPA) of ethylenediamine-tetraacetic acid (EDTA).

The label may also be a chemiluminescent compound. The presence of the chemiluminescently labeled reagent is then determined by detecting the presence of luminescence that arises during the course of a chemical reaction. Examples of particularly useful chemiluminescent labeling compounds are luminol, isolumino, theromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

Likewise, a bioluminescent compound may be used for labeling. Bioluminescence is a type of chemiluminescence found in biological systems in which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of luminescence. Important bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

Enzyme labels, such as horseradish peroxidase and alkaline phosphatase, are preferred. When an enzyme label is used, the signal producing system must also include a substrate for the enzyme. If the enzymatic reaction product is not itself detectable, the SPS will include one or more additional reactants so that a detectable product appears.

An enzyme analyte may act as its own label if an enzyme inhibitor is used as a diagnostic reagent.

### *Binding Assay Formats*

Binding assays may be divided into two basic types, heterogeneous and homogeneous. In heterogeneous assays, the interaction between the affinity molecule and the analyte does not affect the label, hence, to determine the amount or presence of analyte, bound label must be separated from free label. In homogeneous assays, the interaction does affect the activity of the label, and therefore analyte levels can be deduced without the need for a separation step.

In one embodiment, the ABM is insolubilized by coupling it to a macromolecular support, and analyte in the sample is allowed to compete with a known quantity of a labeled or specifically labelable analyte analogue. The "analyte



analogue" is a molecule capable of competing with analyte for binding to the ABM, and the term is intended to include analyte itself. It may be labeled already, or it may be labeled subsequently by specifically binding the label to a moiety differentiating the analyte analogue from analyte. The solid and liquid phases are separated, and the labeled analyte analogue in one phase is quantified. The higher the level of analyte analogue in the solid phase, i.e., sticking to the ABM, the lower the level of analyte in the sample.

In a "sandwich assay", both an insolubilized ABM, and a labeled ABM are employed. The analyte is captured by the insolubilized ABM and is tagged by the labeled ABM, forming a ternary complex. The reagents may be added to the sample in either order, or simultaneously. The ABMs may be the same or different. The amount of labeled ABM in the ternary complex is directly proportional to the amount of analyte in the sample.

The two embodiments described above are both heterogeneous assays. However, homogeneous assays are conceivable. The key is that the label be affected by whether or not the complex is formed.

#### Conjugation Methods

A label may be conjugated, directly or indirectly (e.g., through a labeled anti-ABM antibody), covalently (e.g., with SPDP) or noncovalently, to the ABM, to produce a diagnostic reagent. Similarly, the ABM may be conjugated to a solid phase support to form a solid phase ("capture") diagnostic reagent.

Suitable supports include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, agaroses, and magnetite. The nature of the carrier can be either soluble to some extent or insoluble for the purposes of the present invention.

The support material may have virtually any possible structural configuration so long as the coupled molecule is capable of binding to its target. Thus the support configuration may be spherical, as in a bead, or

cylindrical, as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc.

## 5 Biological Assays

A biological assay measures or detects a biological response of a biological entity to a substance.

The biological entity may be a whole organism, an isolated organ or tissue, freshly isolated cells, an  
10 immortalized cell line, or a subcellular component (such as a membrane; this term should not be construed as including an isolated receptor). The entity may be, or may be derived from, an organism which occurs in nature, or which is modified in some way. Modifications may be genetic  
15 (including radiation and chemical mutants, and genetic engineering) or somatic (e.g., surgical, chemical, etc.). In the case of a multicellular entity, the modifications may affect some or all cells. The entity need not be the target organism, or a derivative thereof, if there is a reasonable  
20 correlation between bioassay activity in the assay entity and biological activity in the target organism.

The entity is placed in a particular environment, which may be more or less natural. For example, a culture medium may, but need not, contain serum or serum substitutes, and  
25 it may, but need not, include a support matrix of some kind, it may be still, or agitated. It may contain particular biological or chemical agents, or have particular physical parameters (e.g., temperature), that are intended to nourish or challenge the biological entity.

30 There must also be a detectable biological marker for the response. At the cellular level, the most common markers are cell survival and proliferation, cell behavior (clustering, motility), cell morphology (shape, color), and biochemical activity (overall DNA synthesis, overall protein  
35 synthesis, and specific metabolic activities, such as utilization of particular nutrients, e.g., consumption of oxygen, production of CO<sub>2</sub>, production of organic acids, uptake or discharge of ions).

The direct signal produced by the biological marker may be transformed by a signal producing system into a different signal which is more observable, for example, a fluorescent or colorimetric signal.

5       The entity, environment, marker and signal producing system are chosen to achieve a clinically acceptable level of sensitivity, specificity and accuracy.

10       In some cases, the goal will be to identify substances which mediate the biological activity of a natural biological entity, and the assay is carried out directly with that entity. In other cases, the biological entity is used simply as a model of some more complex (or otherwise inconvenient to work with) biological entity. In that event, the model biological entity is used because activity  
15       in the model system is considered more predictive of activity in the ultimate natural biological entity than is simple binding activity in an in vitro system. The model entity is used instead of the ultimate entity because the former is more expensive or slower to work with, or because  
20       ethical considerations forbid working with the ultimate entity yet.

25       The model entity may be naturally occurring, if the model entity usefully models the ultimate entity under some conditions. Or it may be non-naturally occurring, with modifications that increase its resemblance to the ultimate entity.

Transgenic animals, such as transgenic mice, rats, and rabbits, have been found useful as model systems.

30       In cell-based model assays, where the biological activity is mediated by binding to a receptor (target protein), the receptor may be functionally connected to a signal (biological marker) producing system, which may be endogenous or exogenous to the cell. There are a number of techniques of doing this.

#### 35       "Zero-Hybrid" Systems

In these systems, the binding of a peptide to the target protein results in a screenable or selectable phenotypic change, without resort to fusing the target

protein (or a ligand binding moiety thereof) to an endogenous protein. It may be that the target protein is endogenous to the host cell, or is substantially identical to an endogenous receptor so that it can take advantage of the latter's native signal transduction pathway. Or sufficient elements of the signal transduction pathway normally associated with the target protein may be engineered into the cell so that the cell signals binding to the target protein.

#### "One-Hybrid" Systems

In these systems, a chimera receptor, a hybrid of the target protein and an endogenous receptor, is used. The chimeric receptor has the ligand binding characteristics of the target protein and the signal transduction characteristics of the endogenous receptor. Thus, the normal signal transduction pathway of the endogenous receptor is subverted.

Preferably, the endogenous receptor is inactivated, or the conditions of the assay avoid activation of the endogenous receptor, to improve the signal-to-noise ratio.

See Fowlkes USP 5,789,184 for a yeast system.

Another type of "one-hybrid" system combines a peptide: DNA-binding domain fusion with an unfused target receptor that possesses an activation domain.

#### "Two-Hybrid" System

In a preferred embodiment, the cell-based assay is a two hybrid system. This term implies that the ligand is incorporated into a first hybrid protein, and the receptor into a second hybrid protein. The first hybrid also comprises component A of a signal generating system, and the second hybrid comprises component B of that system. Components A and B, by themselves, are insufficient to generate a signal. However, if the ligand binds the receptor, components A and B are brought into sufficiently close proximity so that they can cooperate to generate a signal.

Components A and B may naturally occur, or be substantially identical to moieties which naturally occur, as components of a single naturally occurring biomolecule, or they may naturally occur, or be substantially identical to moieties which naturally occur, as separate naturally occurring biomolecules which interact in nature.

#### Two-Hybrid System: Transcription Factor Type

In a preferred "two-hybrid" embodiment, one member of a peptide ligand:receptor binding pair is expressed as a fusion to a DNA-binding domain (DBD) from a transcription factor (this fusion protein is called the "bait"), and the other is expressed as a fusion to a transactivation domain (TAD) (this fusion protein is called the "fish", the "prey", or the "catch"). The transactivation domain should be complementary to the DNA-binding domain, i.e., it should interact with the latter so as to activate transcription of a specially designed reporter gene that carries a binding site for the DNA-binding domain. Naturally, the two fusion proteins must likewise be complementary.

This complementarity may be achieved by use of the complementary and separable DNA-binding and transcriptional activator domains of a single transcriptional activator protein, or one may use complementary domains derived from different proteins. The domains may be identical to the native domains, or mutants thereof. The assay members may be fused directly to the DBD or TAD, or fused through an intermediated linker.

The target DNA operator may be the native operator sequence, or a mutant operator. Mutations in the operator may be coordinated with mutations in the DBD and the TAD. An example of a suitable transcription activation system is one comprising the DNA-binding domain from the bacterial repressor LexA and the activation domain from the yeast transcription factor Gal4, with the reporter gene operably linked to the LexA operator.

It is not necessary to employ the intact target receptor; just the ligand-binding moiety is sufficient.

The two fusion proteins may be expressed from the same or different vectors. Likewise, the activatable reporter gene may be expressed from the same vector as either fusion protein (or both proteins), or from a third vector.

5        Potential DNA-binding domains include Gal4, LexA, and mutant domains substantially identical to the above.

Potential activation domains include E. coli B42, Gal4 activation domain II, and HSV VP16, and mutant domains substantially identical to the above.

10       Potential operators include the native operators for the desired activation domain, and mutant domains substantially identical to the native operator.

The fusion proteins may comprise nuclear localization signals.

15       The assay system will include a signal producing system, too. The first element of this system is a reporter gene operably linked to an operator responsive to the DBD and TAD of choice. The expression of this reporter gene will result, directly or indirectly, in a selectable or  
20       screenable phenotype (the signal). The signal producing system may include, besides the reporter gene, additional genetic or biochemical elements which cooperate in the production of the signal. Such an element could be, for example, a selective agent in the cell growth medium. There  
25       may be more than one signal producing system, and the system may include more than one reporter gene.

The sensitivity of the system may be adjusted by, e.g., use of competitive inhibitors of any step in the activation or signal production process, increasing or decreasing the  
30       number of operators, using a stronger or weaker DBD or TAD, etc.

When the signal is the death or survival of the cell in question, or proliferation or nonproliferation of the cell in question, the assay is said to be a selection. When the  
35       signal merely results in a detectable phenotype by which the signaling cell may be differentiated from the same cell in a nonsignaling state (either way being a living cell), the assay is a screen. However, the term "screening assay" may be used in a broader sense to include a selection. When the

narrower sense is intended, we will use the term "nonselective screen".

Various screening and selection systems are discussed in Ladner, USP 5,198,346.

5        Screening and selection may be for or against the peptide: target protein or compound:target protein interaction.

10       Preferred assay cells are microbial (bacterial, yeast, algal, protozoal), invertebrate, vertebrate (esp. mammalian, particularly human). The best developed two-hybrid assays are yeast and mammalian systems.

15       Normally, two hybrid assays are used to determine whether a protein X and a protein Y interact, by virtue of their ability to reconstitute the interaction of the DBD and the TAD. However, augmented two-hybrid assays have been used to detect interactions that depend on a third, non-protein ligand.

20       For more guidance on two-hybrid assays, see Brent and Finley, Jr., Ann. Rev. Genet., 31:663-704 (1997); Fremont-Racine, et al., Nature Genetics, 277-281 (16 July 1997); Allen, et al., TIBS, 511-16 (Dec. 1995); LeCrenier, et al., BioEssays, 20:1-6 (1998); Xu, et al., Proc. Nat. Acad. sci. (USA), 94:12473-8 (Nov. 1992); Esotak, et al., Mol. Cell. Biol., 15:5820-9 (1995); Yang, et al., Nucleic Acids Res., 23:1152-6 (1995); Bendixen, et al., Nucleic Acids Res., 22:1778-9 (1994); Fuller, et al., BioTechniques, 25:85-92 (July 1998); Cohen, et al., PNAS (USA) 95:14272-7 (1998); Kolonin and Finley, Jr., PNAS (USA) 95:14266-71 (1998). See also Vasavada, et al., PNAS (USA), 88:10686-90 (1991) (contingent replication assay), and Rehrauer, et al., J. Biol. Chem., 271:23865-73 (1996) (LexA repressor cleavage assay).

#### Two-Hybrid Systems: reporter Enzyme type

35       In another embodiment, the components A and B reconstitute an enzyme which is not a transcription factor.

As in the last example, the effect of the reconstitution of the enzyme is a phenotypic change which may be a screenable change, a selectable change, or both.

#### 5     In vivo Diagnostic Uses

Radio-labeled ABM may be administered to the human or animal subject. Administration is typically by injection, e.g., intravenous or arterial or other means of administration in a quantity sufficient to permit subsequent  
10     dynamic and/or static imaging using suitable radio-detecting devices. The dosage is the smallest amount capable of providing a diagnostically effective image, and may be determined by means conventional in the art, using known radio-imaging agents as a guide.

15     Typically, the imaging is carried out on the whole body of the subject, or on that portion of the body or organ relevant to the condition or disease under study. The amount of radio-labeled ABM accumulated at a given point in time in relevant target organs can then be quantified.

20     A particularly suitable radio-detecting device is a scintillation camera, such as a gamma camera. A scintillation camera is a stationary device that can be used to image distribution of radio-labeled ABM. The detection device in the camera senses the radioactive decay, the  
25     distribution of which can be recorded. Data produced by the imaging system can be digitized. The digitized information can be analyzed over time discontinuously or continuously. The digitized data can be processed to produce images, called frames, of the pattern of uptake of the radio-labeled  
30     ABM in the target organ at a discrete point in time. In most continuous (dynamic) studies, quantitative data is obtained by observing changes in distributions of radioactive decay in target organs over time. In other words, a time-activity analysis of the data will illustrate  
35     uptake through clearance of the radio-labeled binding protein by the target organs with time.

Various factors should be taken into consideration in selecting an appropriate radioisotope. The radioisotope must be selected with a view to obtaining good quality



resolution upon imaging, should be safe for diagnostic use in humans and animals, and should preferably have a short physical half-life so as to decrease the amount of radiation received by the body. The radioisotope used should preferably be pharmacologically inert, and, in the quantities administered, should not have any substantial physiological effect.

The ABM may be radio-labeled with different isotopes of iodine, for example  $^{123}\text{I}$ ,  $^{125}\text{I}$ , or  $^{131}\text{I}$  (see for example, U.S. Patent 4,609,725). The extent of radio-labeling must, however be monitored, since it will affect the calculations made based on the imaging results (i.e. a diiodinated ABM will result in twice the radiation count of a similar monoiodinated ABM over the same time frame).

In applications to human subjects, it may be desirable to use radioisotopes other than  $^{125}\text{I}$  for labeling in order to decrease the total dosimetry exposure of the human body and to optimize the detectability of the labeled molecule (though this radioisotope can be used if circumstances require). Ready availability for clinical use is also a factor. Accordingly, for human applications, preferred radio-labels are for example,  $^{99\text{m}}\text{Tc}$ ,  $^{67}\text{Ga}$ ,  $^{68}\text{Ga}$ ,  $^{90}\text{Y}$ ,  $^{111}\text{In}$ ,  $^{113\text{m}}\text{In}$ ,  $^{123}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$  or  $^{211}\text{At}$ .

The radio-labeled ABM may be prepared by various methods. These include radio-halogenation by the chloramine - T method or the lactoperoxidase method and subsequent purification by HPLC (high pressure liquid chromatography), for example as described by J. Gutkowska et al in "Endocrinology and Metabolism Clinics of America: (1987) 16 (1):183. Other known methods of radio-labeling can be used, such as IODOBEADS™.

There are a number of different methods of delivering the radio-labeled ABM to the end-user. It may be administered by any means that enables the active agent to reach the agent's site of action in the body of a mammal. Because proteins are subject to being digested when administered orally, parenteral administration, i.e., intravenous, subcutaneous, intramuscular, would ordinarily

be used to optimize absorption of an ABM, such as an antibody, which is a protein.

**EXAMPLES**

We are utilizing a mouse model of diet-induced obesity that progresses to diabetes. The diet is high in fat and has been documented to lead to diabetes in C57BL/6J mice (Surwit et al., 1988). After weaning, C57BL/6J mice were fed either the high fat diet or a standard lab chow diet for 16 weeks. Body weight was monitored bi-weekly. Fasting glucose and insulin levels were measured after 2, 4, 8, and 16 weeks on the diets. At each time point, several diabetic and control mice were sacrificed and a number of tissues collected. For further analysis, RNA was extracted from the gastrocnemius muscles at each time point and used in DNA microarray analyses.

**Animal Models.**

Obesity and subsequent hyperinsulinemia and hyperglycemia were induced by feeding a group of 3 week old mice (50 C57BL/6 males) a high-fat diet (Bio-Serve, Frenchtown, NJ, #F1850 High Carbohydrate-High Fat; 56% of calories from fat, 16% from protein and 27% from carbohydrates). Another group of 3 week old mice (20 C57BL/6 males) were fed the normal control diet (PMI Nutrition International Inc., Brentwood, MO, Prolab RMH3000; 14% of calories from fat, 16% from protein and 60% from carbohydrates). The mice were placed onto the respective diets immediately following weaning. Animal weights were determined weekly. Fasting blood-glucose and plasma insulin measurements were determined after 2, 4, 8 and 16 weeks on the respective diets.

The day after obtaining body weight measurements at the indicated time points, mice were fasted 8 hours and blood glucose concentrations were measured via tail blood samples using a One Touch Glucometer (Lifescan). For insulin measurements, blood was collected into heparinized tubes, plasma obtained by centrifugation and insulin concentrations determined using an Ultra-Sensitive Rat Insulin ELISA kit (ALPCO) as instructed by the manufacturer. Values were adjusted by a factor of 1.23 as determined by the manufacturer to correct for species difference in cross-

reactivity with the antibody (bottom panel). Results reflect mean  $\pm$  SE of 50 mice on the HF diet and 20 mice on the Std diet.

Normal weight, normal fasting blood glucose and normal fasting plasma insulin levels are defined as the respective mean values of the animals fed the control diet.

Two of the "most typical" animals were selected for each group (Control, hyperinsulinemic and Diabetic) at each time point ( 2,4, 8, and 16 weeks after commencement of diet) for sacrifice. The selected mice were sacrificed and muscle tissue obtained and immediately processed for RNA isolation.

#### **Fasting Blood Glucose Levels.**

Blood glucose levels was measured from a drop of blood taken from the tip of the tail of fasted (8 hr) mice using a Lifescan Genuine One Touch glucometer. All measurements occurred between 2:00 pm and 5:00 pm.

#### **Plasma insulin measurements.**

Blood was collected from the tail of fasted (8 hr) mice into a heparinized capillary tube and stored on ice. All collections occurred between 2:00 pm and 5:00 pm. Plasma was separated from red blood cells by centrifugation for 10 minutes at 8000 x g and then stored at -20°C. Insulin concentrations were determined using the Rat Insulin ELISA kit and rat insulin standards (ALPCO) essentially as instructed by the manufacturer. Values were adjusted by a factor of 1.23 as determined by the manufacturer to correct for the species difference in cross-reactivity with the antibody.

#### **RNA isolation.**

Total RNA was isolated from muscle (skeletal muscle, specifically, gastrocnemius) of two mice at each time point during the progression of HF diet-induced type 2 diabetes, as well as age-matched controls on the Std diet, using the RNA STAT-60 Total RNA/mRNA Isolation Reagent according to the manufacturer's instructions (Tel-Test, Friendswood, TX).

**Sample Quantification and Quality Assessment**

Total RNA was quantified and assessed for quality on a Bioanalyzer RNA 6000 Nano chip (Agilent). Each chip  
5 contained an interconnected set of gel-filled channels that allowed for molecular sieving of nucleic acids. Pin-electrodes in the chip were used to create electrokinetic forces capable of driving molecules through these micro-channels to perform electrophoretic separations. Ribosomal  
10 peaks were measured by fluorescence signal and displayed in an electropherogram. A successful total RNA sample featured 2 distinct ribosomal peaks (18S and 28S rRNA).

**Biotinylated cRNA Hybridization Target.**

15 Total RNA was prepared for use as a hybridization target as described in the manufacturer's instructions for CodeLink Expression Bioarrays(TM) (Amersham Biosciences). The CodeLink Expression Bioarrays utilize nucleic acid hybridization of a biotin-labeled complementary RNA(cRNA)  
20 target with DNA oligonucleotide probes attached to a gel matrix.

The biotin-labeled cRNA target is prepared by a linear amplification method. Poly (A) + RNA (within the total RNA population) is primed for reverse transcription by a DNA  
25 oligonucleotide containing a T7 RNA polymerase promoter 5' to a (dT) 24 sequence. After second-strand cDNA synthesis, the cDNA serves as the template in an *in vitro* transcription (IVT) reaction to produce the target cRNA. The IVT is performed in the presence of biotinylated nucleotides to  
30 label the target cRNA. This procedure results in a 50-200 fold linear amplification of the input poly (A) + RNA.

**Hybridization Probes.**

35 The oligonucleotide probes were provided by the Codelink Uniset Mouse I Bioarray (Amersham, product code 300013). Amine-terminated oligonucleotide probes are attached to a three-dimensional polyacrylamide gel matrix. There are 10,000 oligonucleotide probes, each specific to a well-characterized mouse gene. Each mouse gene is

representative of a unique gene cluster from the fourth quarter 2001 Genbank Unigene build. There are also 500 control probes.

The sequences of the probes are proprietary to  
5 Amersham. However, for each probe, Amersham identifies the corresponding mouse gene by NCBI accession number, OGS, LocusLink, Unigene Cluster ID, and description (name). This information should be available from Amersham. In the case of the differentially expressed probes, this  
10 information is duplicated in master table 1. For the complete list, see [http://www4.amershambiosciences.com/aptrix/upp01077.nsf/Content/codelink\\_literature](http://www4.amershambiosciences.com/aptrix/upp01077.nsf/Content/codelink_literature)

15 Under "Gene Lists", select "Uniset Mouse I", and a gene list, in Excel format, can be downloaded.

### **Hybridization**

Using the cRNA target, the hybridization reaction  
20 mixture is prepared and loaded into array chambers for bioarray processing as set forth in the manufacturer's instructions for CodeLink Gene Expression Bioarrays™ (Amersham Biosciences). Each sample is hybridized to an individual microarray. Hybridization is at 37°C. The  
25 hybridization buffer is prepared as set forth in the Motorola instructions. Hybridization to the microarray is detected with an avidinated fluorescent reagent, Streptavidin-Alexa Fluor® 647 (Amersham).

### **Mouse Gene Expression Analysis**

30 Processed arrays were scanned using a GenePix 4000B Microarray Scanner (Axon Instruments, Inc.); array images were acquired using the Amersham CodeLink™ Analysis Software (Release 2.2). The Amersham CodeLink™ Analysis Software  
35 gives an integrated optical density (IOD) value for every spot; a unique background value for that spot is subtracted, resulting in "raw" data points. Individual chips are then normalized by the Amersham Codelink™ software according to the median raw intensity for all 10,000 genes. A negative

control threshold (0.2) is also calculated according to the control probes. The expression data was analyzed to identify genes whose expression levels changed significantly with respect to:

5

Normal mice compared to hyperinsulinemic mice at 2, 4, 8 and 16 weeks on normal vs. high-fat diet.

10

Normal mice compared to hyperinsulinemic/hyperglycemic mice at 2, 4, 8 and 16 weeks on normal vs. high-fat diet.

15

Hyperinsulinemic compared to hyperinsulinemic/hyperglycemic mice at 2, 4, 8 and 16 weeks on high-fat diets.

20

**Database Searches** Nucleotide sequences and predicted amino acid sequences were compared to public domain databases using the Blast 2.0 program (National Center for Biotechnology Information, National Institutes of Health). Nucleotide sequences were displayed using ABI prism Edit View 1.0.1 (PE Applied Biosystems, Foster City, CA).

25

Nucleotide database searches were conducted with the then current version of BLASTN 2.0.12, see Altschul, et al., "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res., 25:3389-3402 (1997). Searches employed the default parameters, unless otherwise stated.

30

For blastN searches, the default was the blastN matrix (1,-3), with gap penalties of 5 for existence and 2 for extension.

35

Protein database searches were conducted with the then-current version of BLAST X, see Altschul et al. (1997), supra. Searches employed the default parameters, unless otherwise stated. The scoring matrix was BLOSUM62, with gap costs of 11 for existence and 1 for extension. The standard low complexity filter was used.

"ref" indicates that NCBI's RefSeq is the source database. The identifier that follows is a RefSeq accession

number, not a GenBank accession number. "RefSeq sequences are derived from GenBank and provide non-redundant curated data representing our current knowledge of known genes. Some records include additional sequence information that was never submitted to an archival database but is available in the literature. A small number of sequences are provided through collaboration; the underlying primary sequence data is available in GenBank, but may not be available in any one GenBank record. RefSeq sequences are not submitted primary sequences. RefSeq records are owned by NCBI and therefore can be updated as needed to maintain current annotation or to incorporate additional sequence information." See also <http://www.ncbi.nlm.nih.gov/LocusLink/refseq.html>

It will be appreciated by those in the art that the exact results of a database search will change from day to day, as new sequences are added. Also, if you query with a longer version of the original sequence, the results will change. The results given here were obtained at one time and no guarantee is made that the exact same hits would be obtained in a search on the filing date. However, if an alignment between a particular query sequence and a particular database sequence is discussed, that alignment should not change (if the parameters and sequences remain unchanged).

#### **Northern Analysis.**

Northern analysis may be used to confirm the results. Favorable and unfavorable genes, identified as described above, or fragments thereof, will be used as probes in Northern hybridization analyses to confirm their differential expression. Total RNA isolated from subject mice will be resolved by agarose gel electrophoresis through a 1% agarose, 1 % formaldehyde denaturing gel, transferred to positively charged nylon membrane, and hybridized to a probe labeled with [32P] dCTP that was generated from the aforementioned gene or fragment using the Random Primed DNA Labeling Kit (Roche, Palo Alto, CA), or to a probe labeled with digoxigenin (Roche Molecular Biochemicals,



Indianapolis, IN), according to the manufacturer's instructions.

#### **Real-Time RNA Analysis.**

5 Real-time RNA analysis may also be used for confirmation. For "real-time" RNA analysis, RNA will be converted to cDNA and then probed with gene-specific primers made for each clone. "Real-time" incorporation of fluorescent dye will be measured to determine the amount of  
10 specific transcript present in each sample. Sample differences (control vs. hyperinsulinemic, hyperinsulinemic vs. diabetic, or control vs. diabetic) will be evaluated. Confirmation using several independent animals is desirable.

#### **In situ Hybridization**

15 Another form of confirmation may be provided by nonisotopic *in situ* hybridizations (NISH) on selected human (obtained by Tissue Informatics) and mouse tissues using cRNA probes generated from mouse genes found to be up- or  
20 down-regulated during the disease progression. *In situ* hybridizations may also be performed on mouse tissues using cRNA probes generated from differentially expressed DNAs. These cRNA's will hybridize to their corresponding messenger RNA's present in cells and will provide information  
25 regarding the particular cell types within a tissue that is expressing the particular gene as well as the relative level of gene expression. The cRNA probes may be generated by *in vitro* transcription of template cDNA by Sp6 or T7 RNA polymerase in the presence of digoxigenin-11-UTP (Roche  
30 Molecular Biochemicals, Mannheim, Germany; Pardue, M.L. 1985. In: *In situ* hybridization, Nucleic acid hybridization, a practical approach: IRL Press, Oxford, 179-202).

#### **Transgenic Animals.**

35 Transgenic expression may be used to confirm the results. In one embodiment, a mouse is engineered to overexpress the favorable or unfavorable mouse gene in question. In another embodiment, a mouse is engineered to express the

corresponding favorable or unfavorable human gene. In a third embodiment, a nonhuman animal other than a mouse, such as a rat, rabbit, goat, sheep or pig, is engineered to express the favorable or unfavorable mouse or human gene.

5

### **Hyperquantitative Tissue Analysis**

In addition to gene expression analysis the tissue sections can also be analyzed using TissueInformatics, Inc.'s TissueAnalytics™ software. A single representative section may be cut from each tissue block, placed on a slide, and stained with H&E. Digital images of each slide may be acquired using a research microscope and digital camera (Olympus E600 microscope and Sony DKC-ST5). These images may be acquired at 20x magnification with a resolution of 0.64 mm/pixel. A hyperquantitative analysis may be performed on the resulting images: First a digital image analysis can identify and annotate structural objects in a tissue using machine vision. These objects, which are constituents of the tissue, can be annotated because they are visually identifiable and have a biological meaning. Subsequently a quantification of these structures regarding their geometric properties like area or stain intensities and their relationship to the field of view or per unit area in terms of a % coverage may be performed. Features or parameters for hyper-quantification are specific for each tissue, and may also include relations between features, measures of overall heterogeneity, including orientation, relative locations, and textures.

### **Correlation Analysis**

Mathematical statistics provides a rich set of additional tools to analyze time resolved data sets of hyper-quantitative and gene expression profiles for similarities, including rank correlation, the calculation of regression and correlation coefficients, and clustering. Continuous functions may also be fitted through the data points of individual gene and tissue feature data. Relation between gene expression and hyper-quantitative tissue data may be

35

linear or non-linear, in synchronous or asynchronous arrangements.

## 5    **Example 1**

Obesity is increasing at an alarming rate in the United States. In parallel, the incidence of type II diabetes is also rising. We are interested in defining alterations in gene expression that correlate with the development of these conditions in the hopes of reversing these dangerous trends.

10    Insulin plays a major role in regulating blood glucose levels. It stimulates the uptake of glucose in adipose tissue and striated muscle for storage as intracellular triglycerides and glycogen. Insulin also inhibits the  
15    release of glucose from the liver. Normally, this would prevent the rise in blood sugar concentration that occurs after eating. However, in the early stages of type 2 diabetes, resistance to insulin is seen.

Muscle plays a major role in glucose metabolism. Thus, it  
20    also is a major contributor to the development of type 2 diabetes. In normal situations, muscle cells respond to increasing levels of insulin by increasing glucose uptake from the bloodstream. However, during the very early stages of type 2 diabetes, muscle tissue becomes resistant to  
25    insulin, requiring the pancreatic beta cells to increase insulin secretion. Eventually, the beta cells become unable to compensate for this increasing insulin resistance from muscle and other cells, and insulin production drops. Thus, clinical type 2 diabetes results from the combination of  
30    insulin resistance and impaired beta cell function.

Defects in muscle glycogen synthesis are known to play a role in the development of insulin resistance (Petersen and Shulman, 2002). At least three steps - those mediated by glycogen synthase, hexokinase, and GLUT4 - have been  
35    reported to be defective in patients with type 2 diabetes. Fatty acids also can induce insulin resistance, and it has been suggested that this was a consequence of altered insulin signaling through PI3-kinase.

We are utilizing a mouse model of diet-induced obesity that progresses to diabetes. The diet is high in fat, an increasing component in the U.S. diet, and has been documented to lead to diabetes in C57BL/6J mice (Surwit et al., 1988). After weaning, C57BL/6J mice were fed either the high fat diet or a standard lab chow diet for 16 weeks. Body weight was monitored bi-weekly. Fasting glucose and insulin levels were measured after 2, 4, 8, and 16 weeks on the diets.

Consumption of the HF diet resulted in significant, progressive increases in body weight and fasting insulin levels in comparison to consumption of the Std diet. Fasting glucose levels of mice on the HF diet were dramatically increased at the first time point assayed (2 weeks) and remained high through the duration of the experiment (16 weeks).

At each time point, several diabetic and control mice were sacrificed and a number of tissues collected. RNA was extracted from the gastrocnemius muscle at each time point.

In order to identify additional muscle genes involved in the development of type 2 diabetes, we used microarray analysis to compare RNA expression levels of 10,000 genes in muscle of high fat diet fed and control diet fed mice at various time points in the progression of type 2 diabetes. Microarray analysis provides a more global picture of gene regulation, allowing the identification of families or groups of genes showing similar expression patterns that potentially imply similar or coordinated roles in disease progression.

Consumption of the HF diet resulted in significant, progressive increases in body weight and fasting insulin levels in comparison to consumption of the Std diet. Fasting glucose levels of mice on the HF diet were dramatically increased at the first time point assayed (2 weeks) and remained high through the duration of the experiment (16 weeks).

Of 10,000 genes analyzed, 121 were up-regulated but only 7 down-regulated greater than two-fold in the diabetic

relative to non-diabetic mice. These genes are listed in Master Table 1.

This distribution of up- and down-regulated genes was much different from that seen for other organs (liver, pancreas, and white adipose tissue) where there was a much closer balance between the number of up- and down-regulated genes. Actin, alpha, cardiac (Actc1, NM\_009608) was one of the most down-regulated genes when comparing HF to Std mice. It was consistently expressed at lower levels in the HF diabetic mice in comparison to the Std mice and also steadily decreased over the 16 week study.

### Example 2

Interestingly, further analysis of the time points and exploration of gene pathways and functionally related genes revealed a subset of actin-related and actin-binding genes exhibiting a consistent decrease in expression (although less than two-fold) in the diabetic mice; 9 of 37 functionally related genes were decreased in diabetic muscle at all four time points and an additional 9 were decreased at three of the four time points. Only two of these genes had been included in the original list of 7 down-regulated genes using the two-fold cut-off criterion.

It is possible that this subtle but coordinated down-regulation of actin-related or actin-binding genes reflects a role in the decreased glucose uptake by skeletal muscle that occurs in diabetes. With nearly half (18 of 37) of the genes in a related family of genes being consistently down-regulated in a study that did not identify a large number of down regulated genes, we feel that actin and genes in actin-related pathways may prove to play key roles in muscle as obesity and diabetes progress.

The actin-related and actin-binding mouse genes in question have been included at the end of Master Table 1, subtable 1A.

## Introduction to Master Tables

The master tables reflect applicants' analysis of the gene chip data.

5

For each probe corresponding to a differentially expressed mouse gene, Master Table 1 identifies

10

Col. 1: The mouse gene (upper) and mouse protein (lower) database accession #s.

Col. 2: The corresponding mouse Unigene Cluster, as of the 4<sup>th</sup> Quarter 2001 build.

15

Col. 3: The behavior (differential expression) observed for the mouse gene. This column identifies the gene as favorable(F) or unfavorable (U) on the basis of its strongest differential behavior at the ages tested. There are three possible comparisons, HI-D, C-HI, and C-D, where C=control (normal), HI=hyperinsulinemic, and D=diabetic. If HI>D, C>HI, or C>D, the behavior for that subject comparison is considered unfavorable. If the inequality is reversed, the behavior for that subject comparison is considered favorable.

20

25

In the Master Table, the numerical value is the ratio of the greater value to the lesser value. If this ratio is at least two fold, the degree of differential expression is considered strong. Usually only mouse genes exhibiting at least one strong differential expression behavior are listed in the Master Table; exceptions are noted in the Examples.

30

35

In Master Table 1, subtables 1A and 2A, the fold expression values are negative. Likewise, in subtables 1C and 2C, the fold expression values for the favorable behaviors are negative. This does not have its usual mathematical meaning; it is merely a flag that in at least one comparison (HI-D, C-HI, and C-D), the former value was less than the latter one, i.e., the behavior was favorable. For the purpose of applying the teachings of the specification concerning desired ratios, any negative value

should be converted to a positive one by taking its absolute value.

5 Col. 4: A related human protein, identified by its database  
accession number. Usually, several such proteins are  
identified relative to each mouse gene. These proteins have  
been identified by BLAST searches, as explained in cols. 6-  
8.

10

Col. 5: The name of the related human protein.

Col. 6: The score (in bits) for the alignment performed by  
the BLAST program.

15

Col. 7: The E-value for the alignment performed by the BLAST  
program. It is worth noting that Unigene considers a Blastx  
E Value of less than  $1e-6$  to be a "match" to the reference  
sequence of a cluster.

20

Unless otherwise indicated, the bit score and E-value for  
the alignment is with respect to the alignment of the mouse  
DNA of col. 1 to the human protein of col. 4 by BlastX,  
according to the default parameters.

25

Master Table 1 is divided into three subtables on the basis  
of the behavior in col. 3. If a gene has at least one  
significantly favorable behavior, and no significantly  
unfavorable ones, it is put into Subtable 1A. In the  
30 opposite case, it is put into Subtable 1B. If its behavior  
is mixed, i.e., at least one significantly favorable and at  
least one significantly unfavorable, it is put into Subtable  
1C. Note that this classification is based on the strongest  
observed differential expression behaviors for each of the  
35 three subject comparisons, C-HI, HI-D and C-D.

The corresponding human gene clusters are also of interest.  
These may be obtained in a number of ways. First, one may

search on Unigene

(<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=unigene>)  
for the identified human protein. Review the "hits" (each  
of which is a Unigene record) for those prefixed by "Hs."

- 5 Secondly, one may access the Unigene record for the mouse  
gene cluster (which is given in Master Table 1), and then  
click on "Homologene". This will bring up a new page which  
includes the section "Possible Homologous Genes". One of  
the entries should be a Homo sapiens gene (considered by  
10 Unigene to be the most related human gene); click on its  
Unigene record link.

Additional information of interest may be accessed by  
searching with the mouse gene accession # in the Mouse Gene  
Informatics database, at <http://www.informatics.jax.org/>.



# MASTER TABLE 1 SIGNIFICANTLY DIFFERENTIALLY EXPRESSED MOUSE GENES/PROTEINS AND CORRESPONDING HUMAN PROTEINS

Subtable 1A: Wholly Favorable Genes and Proteins

Mouse Gene Protein	Unigene	Behavior	Human Proteins	Human Protein Name	Score (bits)	E-value
X82786 CAA58026.1	Mm.4078	F:(IR-D) -3.33	NP_002408.2	antigen identified by monoclonal antibody Ki-67; Proliferation-related Ki-67 antigen	1711	0
			P46013	KI67 HUMAN Antigen Ki-67	1711	0
			A48666	cell proliferation antigen Ki-67, long form	1711	0
			CAA46519.1	antigen of the monoclonal antibody Ki-67	1711	0
			CAA46520.1	antigen of the monoclonal antibody Ki-67	1315	0
			B48666	cell proliferation antigen Ki-67, short form	1276	0
NM_013788 NP_038816.1	Mm.90135	F:(IR-D) -2.74	BAB86352.1	GSK-3beta binding protein FRAT1	205	8E-54
			AAH34476.1	frequently rearranged in advanced T-cell lymphomas	204	1E-53
			NP_005470.1	frequently rearranged in advanced T-cell lymphomas	204	2E-53
			Q92837	FRAT1_HUMAN Proto-oncogene FRAT1 (Frequently rearranged in advanced T-cell lymphomas)	204	2E-53
			AAB97096.2	proto-oncogene	204	2E-53
NM_019641 NP_062615.1	Mm.28479	F:(IR-D) -2.54	NP_005554.1	stathmin 1; metablastin; prosolin; oncoprotein 18; phosphoprotein 19; stathmin; leukemia-associated phosphoprotein p18	286	8E-78
			P16949	STN1_HUMAN Stathmin (Phosphoprotein p19) (pp19) (Oncoprotein 18) (Op18) (Leukemia-associated phosphoprotein p18) (pp17) (Prosolin) (Metablastin) (Pr22 protein)	286	8E-78
			A40936	stathmin	286	8E-78
			CAA77660.1	Pr22 protein	286	8E-78
			CAA37391.1	stathmin	286	8E-78
			AAA59971.1	oncoprotein 18	286	8E-78
			AAA59980.1	protein p18	286	8E-78
			CAA64398.1	Pr22	286	8E-78
			CAC16020.1	dJ125I3.1 (leukemia-associated phosphoprotein p18 (stathmin))	286	8E-78
			AAH14353.1	AAH14353 Similar to stathmin 1/oncoprotein 18	285	2E-77

			Q9H169	STN4 HUMAN Stathmin 4 (Stathmin-like protein B3) (RB3)	194	4E-50
			CAC22254.1	RB3 protein	194	4E-50
			CAB66503.1	hypothetical protein	194	4E-50
			NP_110422.2	stathmin-like-protein RB3	194	4E-50
			AAH11520.1	AAH11520 Similar to stathmin-like-protein RB3	194	4E-50
NM_011623	Mm.4237	F:(IR-D)	NP_001058.2	DNA topoisomerase II, alpha isozyme; topoisomerase (DNA) II alpha (170kD); DNA topoisomerase II, 170 kD	194	4E-50
NP_035753.1		-2.33			2463	0
			P11388	TP2A HUMAN DNA topoisomerase II, alpha isozyme	2463	0
			AAC77388.1	topoisomerase II alpha	2463	0
			AAA61209.1	DNA topoisomerase II (EC 5.99.1.3)	2462	0
			CAA09762.1	DNA topoisomerase (ATP-hydrolyzing); topoisomerase II alpha	2454	0
			A40493	DNA topoisomerase (ATP-hydrolyzing) (EC 5.99.1.3) alpha	2441	0
			Q02880	TP2B HUMAN DNA topoisomerase II, beta isozyme	1923	0
			A39242	DNA topoisomerase (ATP-hydrolyzing) (EC 5.99.1.3) beta, splice form 2	1923	0
			NP_001059.2	DNA topoisomerase II, beta isozyme; topo II beta; DNA topoisomerase II, 180 kD; topoisomerase (DNA) II beta (180kD)	1923	0
			CAA48197.1	DNA topoisomerase II	1923	0
			AAC77432.1	DNA topoisomerase II beta	1918	0
			AAA61210.1	topoisomerase II	1494	0
AK007688	Mm.41925	F:(IR-D)	NP_076947.1	hypothetical protein MGC2601	457	e-128
AAH37181.1		-2.27				
			CAB56188.1	c380A1.2.1 (novel protein (isoform 1))	457	e-128
			AAH00662.1	Unknown (protein for MGC:2601)	457	e-128
			AAK61247.1	AE006464 15 unknown	457	e-128
			CAB56189.1	c380A1.2.2 (novel protein (isoform 2))	300	3E-81
NM_011593	Mm.8245	F:(IR-D)	CAA26443.1	EPA glycoprotein	270	1E-72
NP_035723.1		-2.18				
			NP_003245.1	tissue inhibitor of metalloproteinase 1 precursor; Erythroid-potentiating activity (tissue inhibitor of metalloproteinases); erythroid potentiating activity	270	1E-72
			P01033	TIM1 HUMAN Metalloproteinase inhibitor 1 precursor (TIMP-1) (Erythroid potentiating activity) (EPA) (Tissue inhibitor of metalloproteinases) (Fibroblast	270	1E-72

					collagenase inhibitor) (Collagenase inhibitor)		
				ZYHUEP	metalloproteinase tissue inhibitor 1 precursor [validated]	270	1E-72
				CAA26902.1	precursor	270	1E-72
				AAA52436.1	prefibroblast collagenase inhibitor	270	1E-72
				AAA63234.1	collagenase inhibitor	270	1E-72
				AAD14009.1	S68252 1 metalloproteinase inhibitor	270	1E-72
				AAH00866.1	AAH00866 tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity, collagenase inhibitor)	270	1E-72
				1107278A	erythroid potentiating activity	270	1E-72
				1308125A	metalloproteinase inhibitor	270	1E-72
				IUEA	B Chain B, Mmp-3TIMP-1 Complex	264	8E-71
				IUEA	D Chain D, Mmp-3TIMP-1 Complex	264	8E-71
				BAA01913.1	tissue inhibitor of metalloproteinases	236	1E-62
				AAH07097.1	AAH07097 tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity, collagenase inhibitor)	221	6E-58
NM_016785 NP_058065.1	Mm.10169	F:(IR-D) -2.18		NP_000358.1	thiopurine S-methyltransferase	376	e-104
				P51580	TPMT HUMAN Thiopurine S-methyltransferase (Thiopurine methyltransferase)	376	e-104
				I57946	thiopurine methyltransferase	376	e-104
				AAB27277.1	thiopurine methyltransferase; TPMT	376	e-104
				AAC50130.1	thiopurine methyltransferase	376	e-104
				AAC50368.1	thiopurine methyltransferase	376	e-104
				AAC51865.1	thiopurine S-methyltransferase	376	e-104
				BAA97037.1	thiopurine S-methyltransferase	376	e-104
				AAH09596.1	AAH09596 thiopurine S-methyltransferase	376	e-104
				AAB71630.1	thiopurine methyltransferase	375	e-104
				AAB71626.1	thiopurine methyltransferase	375	e-104
				AAB80746.1	thiopurine S-methyltransferase	374	e-103
				AAB71629.1	thiopurine methyltransferase	374	e-103
				AAB71627.1	thiopurine methyltransferase	373	e-103
				AAH05339.1	AAH05339 thiopurine S-methyltransferase	372	e-103
				AAB71625.1	thiopurine methyltransferase	371	e-103
				AAB80747.1	thiopurine S-methyltransferase	371	e-130

				AAC50129.1	thiourine methyltransferase		265	9E-84
				XP_031946.2	similar to thiourine methyltransferase		265	6E-83
U08020	Mm.22621	F:(IR-D)		P02452	CA11_HUMAN Collagen alpha 1(I) chain precursor		486	e-136
AAA88912.1		-2.16						
				AAB94054.2	pro alpha 1(I) collagen		486	e-136
				NP_000079.1	alpha 1 type I collagen preproprotein; Collagen I, alpha-1 polypeptide; osteogenesis imperfecta type IV; collagen of skin, tendon and bone, alpha-1 chain		484	e-136
				CAA98968.1	prepro-alpha1(I) collagen		484	e-136
				CGHU1S	collagen alpha 1(I) chain precursor		483	e-136
				AAA51995.1	alpha-1 (I) chain propeptide		482	e-135
				AAH36531.1	Unknown (protein for MGC:33668)		480	e-135
				AAB27856.1	type I collagen pro alpha 1(I) chain propeptide		469	e-131
				CAA29605.1	C-terminal propeptide domain		435	e-121
				CAA29604.1	pro-alpha 1 (II) collagen (313 AA; AA 975-271c)		372	e-102
				NP_001835.2	alpha 1 type II collagen isoform 1; collagen II, alpha-1 polypeptide; cartilage collagen; chondrocalcin, included; COL11A3, formerly		372	e-102
				AAC41772.1	alpha-1 type II collagen		372	e-102
NM_023043	Mm.18075	F:(IR-D)		NP_036541.1	prion gene complex, downstream		283	1E-75
NP_075530.1	0	-2.14						
				Q9UKY0	PRND_HUMAN Prion-like protein doppel precursor (PrPLP) (Prion protein 2)		283	1E-75
				AAF02424.1	AF106918_1 prion-like protein		283	1E-75
				CAB75502.1	dJ1068H6.4 (prion protein like protein doppel)		282	2E-75
				AAG43449.1	prion-like protein		281	3E-75
				AAG43448.1	AF187843_1 doppel protein		246	2E-64
NM_009464	Mm.6254	F:(IR-D)		NP_003347.1	uncoupling protein 3, isoform UCP3L		531	e-151
NP_033490.1		-2.07						
				P55916	UCP3_HUMAN Mitochondrial uncoupling protein 3 (UCP 3)		531	e-151
				JC5522	uncoupling protein UCP3, mitochondrial		531	e-151
				AAC51367.1	UCP3		531	e-151
				AAC51369.1	uncoupling protein 3		531	e-151

				AAC51767.1	uncoupling protein-3	531 e-151
				AAG02284.1	AF050113_1 uncoupling protein-3	531 e-151
				AAC18822.1	uncoupling protein 3	525 e-149
				AAC51785.1	uncoupling protein 3	510 e-144
				NP_073714.1	uncoupling protein 3, isoform UCP3S	464 e-131
				AAC51356.1	UCP3S	464 e-131
				AAB48411.1	uncoupling protein-2	457 e-129
				NP_003346.2	uncoupling protein 2	456 e-128
				P55851	UCP2_HUMAN Mitochondrial uncoupling protein 2 (UCP 2) (UCPH)	456 e-128
				AAC51336.1	UCP2	456 e-128
				AAC39690.1	uncoupling protein 2	456 e-128
				AAD21151.1	uncoupling protein-2	456 e-128
				AAH11737.1	AAH11737 uncoupling protein 2 (mitochondrial, proton carrier)	456 e-128
				AAB53091.1	uncoupling protein homolog	456 e-128
				CAA11402.1	uncoupling protein 2	456 e-128
				NP_068605.1	uncoupling protein 1; mitochondrial brown fat uncoupling protein	345 7E-95
				G01858	uncoupling protein 1, mitochondrial	345 7E-95
				AAAS271.1	uncoupling protein	345 7E-95
				P25874	UCP1_HUMAN Mitochondrial brown fat uncoupling protein 1 (UCP 1) (Thermogenin)	342 6E-94
				CAA36214.1	uncoupling protein	342 6E-94
				AAH08392.1	AAH08392 Similar to uncoupling protein 3 (mitochondrial, proton carrier)	214 2E-55
AK014626	Mm.10557	F:(IR-D)		CAC07336.1	dJ137F1.2 (novel member of the potassium channel subfamily K)	309 9E-84
XP_138942.1	1	-2.06				
				NP_115491.1	potassium channel, subfamily K, member 16; pancreatic 2P domain potassium channel TALK-1	285 2E-76
				Q96T55	CIWG HUMAN Potassium channel subfamily K member 16 (TWIK-related alkaline pH activated K+ channel 1) (2P domain potassium channel Talk-1)	285 2E-76
				AAK49532.1	AF358909_1 2P domain potassium channel Talk-1	285 2E-76

NM_010514 NP_034644.1	Mm.3862	F:(IR-D) -2.06	NP_000603.1	insulin-like growth factor 2 (somatomedin A), somatomedin A	255	5E-67
			P01344	IGF2_HUMAN Insulin-like growth factor II precursor (IGF-II) (Somatomedin A)	255	5E-67
			IGHU2	nsulin-like growth factor II precursor [validated]	255	5E-67
			CAA25426.1	IGF-II precursor	255	5E-67
			CAA29516.1	precursor polypeptide (AA -24 to 156)	255	5E-67
			AAA52442.1	preproinsulin-like growth factor II, domains A-E	255	5E-67
			AAA52535.1	insulin-like growth factor	255	5E-67
			AAA52545.1	insulin-like growth factor II precursor	255	5E-67
			AAA60088.1	insulin-like growth factor II	255	5E-67
			AAB34155.1	insulin-like growth factor II; IGF-II	255	5E-67
			AAG17220.1	AF217977 1 unknown	255	5E-67
			AAH00531.1	AAH00531 insulin-like growth factor 2 (somatomedin A)	255	5E-67
			AAM51825.1	AF517226 1 insulin-like growth factor 2 (somatomedin A)	255	5E-67
			I009249A	insulin-like growth factor II precursor	255	5E-67
			I203258B	insulin-like growth factor II	255	5E-67
			AAA52544.1	insulin-like growth factor II precursor	254	1E-66
			I67610	insulin-like growth factor II, domains A-E	250	2E-65
			AAA52443.1	preproinsulin-like growth factor II, domains A-E	250	2E-65
			S02423	insulin-like growth factor II precursor, splice form II	249	3E-65
			CAA27249.1	put. IGF-II	249	3E-65
			CAA29517.1	precursor polypeptide (AA -24 to 140)	223	2E-57
NM_012000 NP_036130.1	Mm.21578	F:(IR-D) -2.09	AAH07725.1	AAH07725 ceroid-lipofuscinosis, neuronal 8 (epilepsy, progressive with mental retardation)	448	e-125
			NP_061764.1	ceroid-lipofuscinosis, neuronal 8 (epilepsy, progressive with mental retardation)	446	e-125
			Q9UBY8	CLN8 HUMAN CLN8 protein	446	e-125
			AAFI3115.1	AF123757 1 putative transmembrane protein	446	e-125
			AAFI3116.1	AF123758 1 putative transmembrane protein	446	e-125
			AAFI3117.1	AF123759 1 putative transmembrane protein	446	e-125
			AAFI3118.1	AF123760 1 putative transmembrane protein	446	e-125
			AAFI3119.1	AF123761 1 putative transmembrane protein	446	e-125

NM_025285 NP_079561.1	Mm.29580	F:(C-IR) -4.72	XP_170521.1	similar to data source:MGD, source key:MGI:98241, evidence:ISS-putative-superiorcervical ganglia, neural specific 10	345 2E-94
			AAH06302.1	AAH06302 Similar to superiorcervical ganglia, neural specific 10	345 2E-94
			NP_008960.1	superiorcervical ganglia, neural specific 10; neuronal growth-associated protein (silencer element); superior cervical ganglia, neural specific 10	342 1E-93
			AAB36428.1	SCG10	342 1E-93
			Q93045	STN2_HUMAN Stathmin 2 (SCG10 protein) (Superior cervical ganglion-10 protein)	342 1E-93
			BAA23326.1	silencer element	342 1E-93
			NP_056978.2	SCG10-like-protein	249 1E-65
			Q9NZ72	STN3_HUMAN Stathmin 3 (SCG10-like protein)	249 1E-65
			AAF35245.1	SCG10 like-protein	249 1E-65
			CAC16222.1	bK3184A7.2 (SCG10-like protein (SCLIP) (ortholog of rabbit neuroplastin-2 (NPC2)))	249 1E-65
			AAH09381.1	AAH09381 Unknown (protein for MGC:16668)	249 1E-65
			AAD12730.1	SCG10-like-protein	248 2E-65
			BAC11252.1	unnamed protein product	245 2E-65
			Q9H169	STN4_HUMAN Stathmin 4 (Stathmin-like protein B3) (RB3)	217 5E-56
			CAC22254.1	RB3 protein	217 5E-56
			CAB66503.1	hypothetical protein	217 5E-56
			NP_110422.2	stathmin-like-protein RB3	206 7E-53
			AAH11520.1	AAH11520 Similar to stathmin-like-protein RB3	206 7E-53
NM_008687 NP_032713.1	Mm.4025	F:(C-IR) -2.69	AAH01283.1	Similar to nuclear factor I/B	808 0
			NP_005587.1	nuclear factor I/B	807 0
			O00712	NFIB_HUMAN Nuclear factor 1 B-type (Nuclear factor 1/B) (NF1-B) (NFI-B) (NF-I/B) (CCAAT-box binding transcription factor) (CTF) (TGGCA-binding protein)	807 0
			AAB41899.1	nuclear factor I-B2	807 0
			AAA93125.1	nuclear factor 1 B-type	507 e-143
			NP_005588.1	nuclear factor I/C (CCAAT-binding transcription factor)	499 e-140
			CAA63440.1	NFI/CAAT-binding transcription factor 5 (CTF5)	499 e-140
			AAH12120.1	nuclear factor I/C (CCAAT-binding transcription factor)	499 e-140





			1209280A	tropomyosin	365 e-101
			P09493	TPM1_HUMAN Tropomyosin 1 alpha chain (Alpha-tropomyosin)	345 8E-95
			A25825	tropomyosin alpha chain, cardiac and skeletal muscle	345 8E-95
			AAA61225.1	skeletal muscle tropomyosin	345 8E-95
			P07951	TPM2_HUMAN Tropomyosin beta chain (Tropomyosin 2) (Beta-tropomyosin)	326 3E-89
			S00922	tropomyosin beta, skeletal muscle	326 3E-89
			CAA29971.1	beta-tropomyosin (AA 1-284)	326 3E-89
			AAH07433.1	AAH07433 Similar to tropomyosin 1 (alpha)	325 7E-89
			NP_689476.1	tropomyosin 3	315 9E-86
			BAC03946.1	unnamed protein product	315 9E-86
			AAA61226.1	skeletal muscle tropomyosin	310 2E-84
			BAB14554.1	unnamed protein product	300 2E-81
			NP_000357.2	tropomyosin 1 (alpha)	281 1E-75
			A27674	tropomyosin 3, fibroblast	281 1E-75
			AAA36771.1	tropomyosin	281 1E-75
			T08796	tropomyosin	278 1E-74
			CAB43309.1	hypothetical protein	278 1E-74
NM_011825	Mm.25760	F:(C-IR)	NP_071914.1	hypothetical protein FLJ21195 similar to protein related to DAC	308 5E-83
NP_035955.1		-2.24			
			BAB15026.1	unnamed protein product	308 5E-83
NM_009831	Mm.2103	F:(C-IR)	NP_004051.1	cyclin G1	543 e-154
NP_033961.1		-2.2			
			P51959	CGG1_HUMAN Cyclin G1 (Cyclin G)	543 e-154
			G02401	cyclin G1	543 e-154
			AAC41977.1	cyclin G1	543 e-154
			AAC50688.1	cyclin G1	543 e-154
			BAA11353.1	cyclin G	543 e-154
			AAH00196.1	cyclin G1	543 e-154
			2210321A	cyclin G1	543 e-154
			AAH07093.	cyclin G1	541 e-154

			BAA13007.1	cyclin G		514 e-146
			CAA54821.1	cyclin G1		462 e-130
			G02523	cyclin G		421 e-117
			AAB03903.1	cyclin G		421 e-117
			AAH32518.1	Similar to cyclin G2		292 8E-79
			NP_004345.1	cyclin G2		292 8E-79
			Q16589	CGG2_HUMAN Cyclin G2		292 8E-79
			AAC41978.1	cyclin G2		292 8E-79
			AAC50689.1	cyclin G2		292 8E-79
			AAN40704.1	cyclin G2		292 8E-79
			2210321B	cyclin G2		292 8E-79
NM_021282	Mm.21758	F:(C-IR) -2.19	NP_000764.1	cytochrome P450, subfamily IIE, polypeptide 1; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase; cytochrome P450, subfamily IIE (ethanol-inducible)		792 0
NP_067257.1		F:(C-D) -2.5				
			P05181	CPE1 HUMAN Cytochrome P450 2E1 (CYP1IE1) (P450-J)		792 0
			A31949	cytochrome P450 2E		792 0
			AAA52155.1	cytochrome P450IIE1		792 0
			AAA35743.1	cytochrome P450j		792 0
			AAF13601.1	AF182276 1 cytochrome P450-2E1		790 0
			AAD13753.1	cytochrome P450 2E1		751 0
			NP_000760.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 19; mephenytoin 4'-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase		557 e-158
			P33261	CPCJ_HUMAN Cytochrome P450 2C19 (CYP1IC19) (P450-11A) (Mephenytoin 4-hydroxylase) (CYP1IC17) (P450-254C)		557 e-158
			AAB59426.1	cytochrome		557 e-158
			NP_000763.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 18; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 17; microsomal monooxygenase; flavoprotein-linked monooxygenase		556 e-158
			AAB59356.1	cytochrome		556 e-158
			P33260	CPCI_HUMAN Cytochrome P450 2C18 (CYP1IC18) (P450-6B/29C)		553 e-157
			A61269	cytochrome P450 2C18		553 e-157
			AAA02630.1	cytochrome P-4502C18		553 e-157

				BAA00123.1	cytochrome P-450		550	e-156
				NP_000762.2	cytochrome P450, subfamily IIC, polypeptide 9; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 10; mephenytoin 4-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase		550	e-156
				P111712	CPC9_HUMAN Cytochrome P450 2C9 (CYP11C9) (P450 PB-1) (P450 MP-4) (S-mephenytoin 4-hydroxylase) (P-450MP)		550	e-156
				B38462	S-mephenytoin 4-hydroxylase (EC 1.14.14.-) cytochrome P450 2C9		550	e-156
				I313295A	cytochrome P450		550	e-156
				F38462	S-mephenytoin 4'-hydroxylase (EC 1.14.14.-) cytochrome P450 2C19		550	e-156
				AAB23864.2	cytochrome P-450		545	e-155
AK019452	Mm.29952	F:(C-IR)	-2.19	NP_078847.1	hypothetical protein FLJ22940		258	9E-69
BAB31728.1								
				AAH01381.1	polymerase (RNA) III (DNA directed) polypeptide K (12.3 kDa)		258	9E-69
				AAH09179.1	hypothetical protein FLJ22940		258	9E-69
				AAK61211.1	AE006462 3 Minus -99 protein		258	9E-69
				BAB15505.1	unnamed protein product		256	4E-68
NM_008832	Mm.42254	F:(C-IR)	-2.18	NP_002628.1	phosphorylase kinase, alpha 1 (muscle); phosphorylase kinase, alpha 1 (muscle), muscle glycogenosis; Phosphorylase kinase, muscle, alpha polypeptide		2244	0
NP_032858.1								
				P46020	KPB1_HUMAN Phosphorylase B kinase alpha regulatory chain, skeletal muscle isoform (Phosphorylase kinase alpha M subunit)		2244	0
				I38111	phosphorylase kinase (EC 2.7.1.38) alpha-1 chain		2244	0
				CAA52083.1	phosphorylase kinase		2244	0
				NP_000283.1	phosphorylase kinase, alpha 2 (liver); Phosphorylase kinase deficiency, liver (glycogen storage disease; phosphorylase kinase, alpha 2 (liver), glycogen storage disease IX		1628	0
				P46019	KPB2_HUMAN Phosphorylase B kinase alpha regulatory chain, liver isoform (Phosphorylase kinase alpha L subunit)		1628	0
				CAA56662.1	phosphorylase kinase		1628	0
				BAA07606.1	phosphorylase kinase alpha subunit		1628	0

			AAD32846.1	phosphorylase kinase alpha subunit	1628 0
			AAH14036.1	AAH14036 Similar to phosphorylase kinase, alpha 2 (liver)	1624 0
			CAB86408.1	dI499B10.2 (phosphorylase kinase, alpha 2 (liver) (PYK))	631 e-180
			AAB27307.1	phosphorylase kinase alpha subunit liver isoform, PHKA2 (EC 2.7.1.38) [human, hepatoma, Peptide Partial, 377 aa]	473 e-132
			S74251	phosphorylase kinase (EC 2.7.1.38) beta chain	461 e-129
			AAH33657.1	Similar to phosphorylase kinase, beta	461 e-129
NM_023831 NP_076320.1	Mm.30006 F:(C-IR) -2.16		CAB96537.1	hypothetical protein	465 e-131
			CAB66868.1	hypothetical protein	465 e-131
			AAH11647.1	AAH11647 Similar to hypothetical protein	465 e-131
			AAH12802.1	AAH12802 Similar to hypothetical protein	465 e-131
			AAH22856.1	hypothetical protein	465 e-131
			NP_064538.2	hypothetical protein FLJ21827	465 e-131
			BAB15146.1	unnamed protein product	465 e-131
AK004839 XP_129259.1	Mm.2605 F:(C-IR) -2.15		NP_006735.1	retinol-binding protein 4, plasma precursor	343 2E-94
			pir  VAHU	plasma retinol-binding protein precursor	343 2E-94
			CAA24959.1	precursor RBP	343 2E-94
			P02753	Plasma retinol-binding protein precursor (PRBP) (RBP) (PRO2222)	341 1E-93
			AAH20633.1	Similar to retinol binding protein 4, plasma	341 1E-93
			XP_005907.5	similar to Plasma retinol-binding protein precursor (PRBP) (RBP) (PRO2222)	341 1E-93
			IRBP	Retinol Binding Protein	340 2E-93
			IBRP	Retinol Binding Protein (Holo Form)	340 2E-93
			IBRQ	Retinol Binding Protein (Apo Form)	340 2E-93
			I401251A	retinol binding protein	340 2E-93
			IQAB	E Chain E, The Structure Of Human Retinol Binding Protein With Its Carrier Protein Transthyretin Reveals Interaction With The Carboxy Terminus Of Rbp	328 9E-90
			IQAB	F Chain F, The Structure Of Human Retinol Binding Protein With Its Carrier Protein Transthyretin Reveals Interaction With The Carboxy Terminus Of Rbp	328 9E-90
			AAF69622.1	AF119917 30 PRO2222	288 6E-78

NM_011823	Mm.89979		CAA26553.1	RBP		199	5E-51
NP_035953.1	F:(C-IR) -2.12		AAD50531.1	AF039686_1 G-protein coupled receptor GPR34		698	0
			NP_005291.1	G protein-coupled receptor 34		697	0
			Q9UPC5	GP34 HUMAN Probable G protein-coupled receptor GPR34		697	0
			AAD17248.1	orphan G protein-coupled receptor		697	0
			BAB55362.1	unnamed protein product		697	0
			AAH20678.1	AAH20678 G protein-coupled receptor 34		697	0
NM_025950	Mm.78875	F:(C-IR) -2.08	CAC12705.1	bA6J24.4 (A novel protein similar to cell division cycle control protein 37(CDC37))		514	e-145
NP_080226.1							
			AAH14133.1	AAH14133 Unknown (protein for MGC:20783)		514	e-145
			NP_060383.1	Hsp90-associating relative of Cdc37; hypothetical protein FLJ20639		513	e-145
			BAA91304.1	unnamed protein product		513	e-145
			BAA91206.1	unnamed protein product		303	1E-81
			NP_008996.1	CDC37 homolog; CDC37 (cell division cycle 37, S. cerevisiae, homolog); CDC37 (S. cerevisiae) homolog		210	9E-54
			Q16543	CC37_HUMAN Hsp90 co-chaperone Cdc37 (Hsp90 chaperone protein kinase-targeting subunit) (p50Cdc37)		210	9E-54
			G02313	CDC37 homolog		210	9E-54
			AAB63979.1	CDC37 homolog		210	9E-54
			AAB04798.1	CDC37 homolog		210	9E-54
			AAH00083.1	AAH00083 CDC37 (cell division cycle 37, S. cerevisiae, homolog)		210	9E-54
			AAH08793.1	AAH08793 CDC37 (cell division cycle 37, S. cerevisiae, homolog)		210	9E-54
NM_008452	Mm.26938	F:(C-IR) -2.05	AAD55891.1	AF134053_1 Kruppel-like factor LKLF		431	e-120
NP_032478.1							
			AAD25076.1	AF123344_1 Kruppel-like zinc finger transcription factor		429	e-120
			NP_057354.1	Kruppel-like factor		429	e-120
			Q9Y5W3	KLF2 HUMAN Kruppel-like factor 2 (Lung kruppel-like factor)		429	e-120
			AAF13295.1	AF205849_1 Kruppel-like factor		429	e-120

			AAC03462.1	EZF			213	5E-55
			O43474	KLF4 HUMAN Kruppel-like factor 4 (Epithelial zinc-finger protein EZF) (Gut-enriched Krueppel-like factor)			213	5E-55
			AAD42165.1	AF105036 1 zinc finger transcription factor GKLF			213	5E-55
			AAH29923.1	Kruppel-like factor 4 (gut)			213	5E-55
			NP_004226.1	Kruppel-like factor 4 (gut); endothelial Kruppel-like zinc finger protein			213	5E-55
			AAB48399.1	hEZF			213	5E-55
			AAH30811.1	Similar to Kruppel-like factor 4 (gut)			213	5E-55
			AAH35342.1	Similar to Kruppel-like factor 2 (lung)			211	3E-54
NM_020007 NP_064391.1	Mm.14199 3	F:(C-IR) -2.04	AAK94915.1	AF401998_1 muscleblind 41kD isoform			509	e-166
			NP_066368.1	muscleblind (Drosophila)-like			546	e-160
			BAA24858.1	KTAA0428			546	e-160
			Q9NR56	MBNL_HUMAN Muscleblind-like protein (Triplet-expansion RNA-binding protein)			537	e-157
			CAA74155.1	MBNL protein			537	e-157
			NP_659002.1	muscleblind-like protein MBL139 isoform 1			449	e-125
			AAM09798.1	AF491866_1 muscleblind-like protein MLP1			449	e-125
			AAM50085.1	muscleblind-like protein MBL139			427	e-119
			NP_060858.2	CHCR isoform G			387	e-106
			Q9NUK0	MBXL_HUMAN Muscleblind-like X-linked protein (Cys3His CCG1-required protein) (HCHCR protein)			387	e-106
			AAL65661.1	CHCR isoform G			387	e-106
			BAB85648.1	hCHCR-G			387	e-106
			CAD20869.1	CHCR protein			387	e-106
			AAM09533.1	AF491305_1 MBLX39			387	e-106
			NP_005748.1	muscleblind-like protein MBL139 isoform 2			377	e-103
			AAC67242.1	zinc finger protein			377	e-103
			BAB85649.1	hCHCR-R			343	1E-93
			CAD20870.1	CHCR protein			343	1E-93
			AAL87670.1	AF467070_1 Cys3His CCG1-required protein isoform R			343	1E-93
			AAK82889.1	AF395876_1 36 kDa muscleblind protein EXP36			286	7E-82
NM_009883	Mm.4863	F:(C-IR)	CAC14276.1	bA112L6.1 (CCAAT/enhancer binding protein (C/EBP), beta)			271	2E-72



			AAA35613.1	plasma protease (CI) inhibitor precursor	632 0
			CAA30469.1	CI inhibitor (AA 155-478) (1 is 2nd base in codon)	517 e-146
			AAA51848.1	CI-inhibitor	454 e-127
			AAA51849.1	CI inhibitor	307 3E-83
NM_011082 NP_035212.1	Mm.4317 F:(C-IR) -2.02		XP_052013.1	similar to polymeric immunoglobulin receptor	930 0
			AAN65630.1	hepatocellular carcinoma associated protein TB6	930 0
			NP_002635.1	polymeric immunoglobulin receptor	927 0
			P01833	PIGR_HUMAN Polymeric-immunoglobulin receptor precursor (Poly-Ig receptor) (PIGR) [Contains: Secretory component]	927 0
			QRHUGS	secretory component precursor [validated]	927 0
			AAB20203.1	transmembrane secretory component; poly-Ig receptor; SC	927 0
			AAB23176.1	transmembrane secretory component; SC; poly-Ig receptor	927 0
			CAA51532.1	Polymeric immunoglobulin receptor	927 0
			AAA36102.1	poly-Ig receptor	817 0
NM_010274 NP_034404.1	Mm.3711 F:(C-IR) -2.01		G02093	glycerol-3-phosphate dehydrogenase (EC 1.1.99.5), mitochondrial precursor	1268 0
			AAB60403.1	glycerol-3-phosphate dehydrogenase	1268 0
			AAC50556.1	glycerol-3-phosphate dehydrogenase	1268 0
			NP_000399.1	glycerol-3-phosphate dehydrogenase 2 (mitochondrial)	1266 0
			P43304	GPDM_HUMAN Glycerol-3-phosphate dehydrogenase, mitochondrial precursor (GPD-M) (GPDH-M)	1266 0
			AAAG65701.1	mitochondrial glycerol-3-phosphate dehydrogenase	1266 0
			AAG33851.1	AF311325 1 glycerol-3-phosphate dehydrogenase 3	1071 0
			AAB50200.1	glycerol-3-phosphate dehydrogenase	684 0
			AAH19874.1	AAH19874 Similar to glycerol-3-phosphate dehydrogenase 2 (mitochondrial)	624 e-178
			XP_092005.2	similar to Glycerol-3-phosphate dehydrogenase, mitochondrial precursor (GPD-M) (GPDH-M)	320 8E-87
NM_010801 NP_034931.1	Mm.10414 F:(C-IR) -2.01		NP_071888.1	myeloid leukemia factor 1	435 e-122



			P58340	MLF1_HUMAN Myeloid leukemia factor 1 (Myelodysplasia-myeloid leukemia factor 1)	435 e-122
			AAA99997.1	t(3;5)(q25.1;p34) fusion gene	435 e-122
			AAH07045.1	AAH07045 myeloid leukemia factor 1	435 e-122
			BAC04885.1	unnamed protein product	396 e-110
			BAB71320.1	unnamed protein product	383 e-106
NM_028784 NP_083060.1	Mm.17403 F:(C-IR) -2.01		CAC36886.1	bA525O21.1 (coagulation factor XIII, A1 polypeptide)	482 e-135
			1F13	A Chain A, Recombinant Human Cellular Coagulation Factor Xiii	482 e-135
			1F13	B Chain B, Recombinant Human Cellular Coagulation Factor Xiii	482 e-135
			1GGT	A Chain A, Coagulation Factor Xiii (A-Subunit Zymogen) (E.C.2.3.2.13) (Protein-Glutamine Gamma-Glutamyltransferase A Chain)	482 e-135
			1GGT	B Chain B, Coagulation Factor Xiii (A-Subunit Zymogen) (E.C.2.3.2.13) (Protein-Glutamine Gamma-Glutamyltransferase A Chain)	482 e-135
			1GGU	B Chain B, Human Factor Xiii With Calcium Bound In The Ion Site	482 e-135
			1GGY	B Chain B, Human Factor Xiii With Ytterbium Bound In The Ion Site	482 e-135
			1QRK	B Chain B, Human Factor Xiii With Strontium Bound In The Ion Site	482 e-135
			1GGY	A Chain A, Human Factor Xiii With Ytterbium Bound In The Ion Site	482 e-135
			1GGU	A Chain A, Human Factor Xiii With Calcium Bound In The Ion Site	482 e-135
			1QRK	A Chain A, Human Factor Xiii With Strontium Bound In The Ion Site	482 e-135
			XP_165833.1	similar to coagulation factor XIII, A1 polypeptide	482 e-135
			AAL12161.1	AF418272 1 coagulation factor XIII, A1 polypeptide	482 e-135
			AAAS2415.1	factor XIII a subunit	481 e-135
			1EVU	A Chain A, Human Factor Xiii With Calcium Bound In The Ion Site	481 e-135
			1EVU	B Chain B, Human Factor Xiii With Calcium Bound In The Ion Site	481 e-135
			NP_000120.1	coagulation factor XIII A1 subunit precursor; Coagulation factor XIII, A polypeptide; Tgase	481 e-135
			AAAS2488.1	clotting factor XIIIa precursor (EC 2.3.2.13)	481 e-135
			P00488	F13A_HUMAN Coagulation factor XIII A chain precursor (Protein-glutamine gamma-glutamyltransferase A chain) (Transglutaminase A chain)	481 e-135
			EKHUX	protein-glutamine gamma-glutamyltransferase (EC 2.3.2.13), plasma	481 e-135
			1FIE	B Chain B, Recombinant Human Coagulation Factor Xiii	481 e-135
			1FIE	A Chain A, Recombinant Human Coagulation Factor Xiii	481 e-135

			AAA52489.1	factor XIII precursor		481 e-135
			AAH27963.1	coagulation factor XIII, A1 polypeptide		480 e-135
NM_010439	Mm.16421	F:(C-IR)	NP_002119.1	high-mobility group box 1; high mobility group box 1; high-mobility group (nonhistone chromosomal) protein 1		324 3E-88
NP_034569.1		-2				
			P09429	HMG1 HUMAN High mobility group protein 1 (HMG-1)		324 3E-88
			S02826	nonhistone chromosomal protein HMG-1		324 3E-88
			CAA31110.1	HMG-1 protein (AA 1-215)		324 3E-88
			AAB08987.1	on-histone chromatin protein HMG1		324 3E-88
			AAH03378.1	AAH03378 high-mobility group (nonhistone chromosomal) protein 1		324 3E-88
			AAH30981.1	high-mobility group (nonhistone chromosomal) protein 1		324 3E-88
			BAA09924.1	HMG-1		321 3E-87
			S29857	nonhistone chromosomal protein HMG-1		318 2E-86
			CAB92731.1	dJ579F20.1 (high-mobility group (nonhistone chromosomal) protein 1-like 1)		310 7E-84
			Q9UGV6	HM1X HUMAN High mobility group protein 1-like 10 (HMG-1L10)		301 2E-81
			CAB62951.1	bK445C9.3 (high-mobility group (nonhistone chromosomal) protein 1-like 10)		301 2E-81
			AAF19244.1	AC007277_1 similar to nonhistone chromosomal protein HMG-1 [Homo sapiens]; probable pseudogene; similar to P09429 (PID:g123369)		285 2E-76
			AAH00903.2	AAH00903 high-mobility group (nonhistone chromosomal) protein 2		283 1E-75
			NP_002120.1	high-mobility group box 2; high-mobility group (nonhistone chromosomal) protein 2		283 1E-75
			P26583	HMG2 HUMAN High mobility group protein 2 (HMG-2)		283 1E-75
			NSHUH2	nonhistone chromosomal protein HMG-2		283 1E-75
			CAA44395.1	HMG-2		283 1E-75
			AAA58659.1	high mobility group 2 protein		283 1E-75
			AAH01063.1	AAH01063 high-mobility group (nonhistone chromosomal) protein 2		283 1E-75
			2001363A	high mobility group protein 2		283 1E-75
			XP_086648.2	similar to dJ579F20.1 (high-mobility group (nonhistone chromosomal) protein 1-like 1)		250 7E-66
			NP_005333.1	high-mobility group box 3; high-mobility group (nonhistone chromosomal) protein 4		244 4E-64
			O15347	HMG4_HUMAN High mobility group protein 4 (HMG-4) (High mobility group protein 2a) (HMG-2a)		244 4E-64
			CAA71143.1	high mobility group protein 2a		244 4E-64

NM_013459 NP_038487.1	Mm.4407	F:(C-IR) -2.13	P00746	CFAD_HUMAN Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adipsin)	370 e-102
			CAC48304.1	adipsin/complement factor D precursor	358 4E-99
			DBHU	complement factor D (EC 3.4.21.46) precursor [validated]	352 5E-97
			1FDP	A Chain A, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	340 1E-93
			1FDP	B Chain B, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	340 1E-93
			1FDP	D Chain D, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	340 1E-93
			1FDP	C Chain C, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	340 1E-93
			AAH34529.1	Unknown (protein for IMAGE:4780594)	340 1E-93
			1DST	Mutant Of Factor D With Enhanced Catalytic Activity	330 1E-90
			1BIO	Human Complement Factor D In Complex With Isatoic Anhydride Inhibitor	329 4E-90
			1DIC	A Chain A, Structure Of 3,4-Dichloroisocoumarin-Inhibited Factor D	329 4E-90
			1DSU	A Chain A, Human Factor D, Complement Activating Enzyme	329 4E-90
			1HFD	Human Complement Factor D In A P21 Crystal Form	329 4E-90
			1DPP	A Chain A, Factor D Inhibited By Diisopropyl Fluorophosphate	329 4E-90
			1DPP	B Chain B, Factor D Inhibited By Diisopropyl Fluorophosphate	329 4E-90
			1DSU	B Chain B, Human Factor D, Complement Activating Enzyme	329 4E-90
			XP_084037.1	similar to Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adipsin)	328 8E-90
			NP_001919.1	adipsin/complement factor D precursor	324 1E-88
			AAA35527.1	adipsin/complement factor D	324 1E-88
AK017926 BAB31006.1	Mm.21697	F:(C-D) 2.38	NP_061931.1	RTP801	372 e-103
			BAA91214.1	unnamed protein product	372 e-103
			AAH07714.1	hypothetical protein	372 e-103
			AAH15236.1	hypothetical protein	372 e-103
			AAL38424.1	RTP801	372 e-103
			AAM10442.1	REDD-1	372 e-103
			CAB66603.1	hypothetical protein	370 e-102

NM_007706 NP_031732.1	Mm.4132 F:(C-D) - 2.03	NP_003868.1	suppressor of cytokine signaling-2; STAT induced STAT inhibitor-2; cytokine-inducible SH2 protein 2	364 e-100
		XP_170547.1	similar to Suppressor of cytokine signaling 2 (SOCS-2) (Cytokine-inducible SH2 protein 2) (CIS-2) (STAT induced STAT inhibitor 2) (SSI-2)	364 e-100
		O14508	SOC2 HUMAN Suppressor of cytokine signaling 2 (SOCS-2) (Cytokine-inducible SH2 protein 2) (CIS-2) (STAT induced STAT inhibitor 2) (SSI-2)	364 e-100
		BAA22429.1	STAT induced STAT inhibitor-2	364 e-100
		AAC34745.1	STAT-induced STAT inhibitor-2	364 e-100
		AAH10399.1	STAT induced STAT inhibitor-2	364 e-100
		JC5626	STAT induced STAT inhibitor 2	361 e-100
		JC5760	cytokine-inducible SH2 protein 2	360 3E-99
		BAA22536.1	CIS2	359 4E-99
		AAC98896.1	suppressor of cytokine signalling-2; HSSOCS-2	350 3E-96
AK017895 XP_132692.1	Mm.56539 F:(C-D) - 2.02	AAC09350.1	unknown	317 e-136
		XP_057054.6	similar to SET domain and mariner transposase fusion gene	317 e-136
		AAH11635.1	Similar to SET domain and mariner transposase fusion gene	317 e-136
		NP_006506.1	SET domain and mariner transposase fusion gene	313 e-135
		AAC52012.1	orf; encodes putative chimeric protein with SET domain in N-terminus with similarity to several other human, Drosophila, nematode and yeast proteins	313 e-135
NM_011638 NP_035768.1	Mm.26069 F:(C-D) - 2.02	NP_003225.1	transferrin receptor (p90, CD71); Transferrin receptor	1196 0
		P02786	TFR1_HUMAN Transferrin receptor protein 1 (TFR1) (TR) (Trf) (CD71 antigen) (T9) (p90)	1196 0
		JXHU	transferrin receptor	1196 0
		CAA25527.1	put. transferrin receptor (aa 1-760)	1196 0
		AAAG1153.1	transferrin receptor	1196 0
		I011297A	transferrin receptor	1196 0
		AAF04564.1	AF187320_1 transferrin receptor	1195 0
		AAH01188.1	AAH01188 transferrin receptor (p90, CD71)	1195 0
		IDE4	C Chain C, Hemochromatosis Protein Hfe Complexed With Transferrin Receptor	1023 0

			1DE4	F Chain F, Hemochromatosis Protein Hfe Complexed With Transferrin Receptor	1023 0
			1DE4	I Chain I, Hemochromatosis Protein Hfe Complexed With Transferrin Receptor	1023 0
			1CX8	A Chain A, Crystal Structure Of The Ectodomain Of Human Transferrin Receptor	1020 0
			1CX8	B Chain B, Crystal Structure Of The Ectodomain Of Human Transferrin Receptor	1020 0
			1CX8	C Chain C, Crystal Structure Of The Ectodomain Of Human Transferrin Receptor	1020 0
			1CX8	D Chain D, Crystal Structure Of The Ectodomain Of Human Transferrin Receptor	1020 0
			1CX8	E Chain E, Crystal Structure Of The Ectodomain Of Human Transferrin Receptor	1020 0
			1CX8	F Chain F, Crystal Structure Of The Ectodomain Of Human Transferrin Receptor	1020 0
			1CX8	G Chain G, Crystal Structure Of The Ectodomain Of Human Transferrin Receptor	1020 0
			1CX8	H Chain H, Crystal Structure Of The Ectodomain Of Human Transferrin Receptor	1020 0
			Q9UP52	TFR2 HUMAN Transferrin receptor protein 2 (TFR2)	545 e-154
			AAD45561.1	AF067864 1 transferrin receptor 2 alpha	545 e-154
			NP_003218.1	transferrin receptor 2	498 e-140
			AAC78796.1	transferrin-receptor2	498 e-140
			BAA91153.1	unnamed protein product	315 2E-85
			AAC83972.1	prostate-specific membrane antigen	228 2E-59
			NP_004467.1	folate hydrolase (prostate-specific membrane antigen) 1; folate hydrolase 1 (prostate-specific membrane antigen)	228 3E-59
			Q04609	FOH1_HUMAN Glutamate carboxypeptidase II (Membrane glutamate carboxypeptidase) (mGCP) (N-acetylated-alpha-linked acidic dipeptidase I) (NAALADase I) (Pteroylpoly-gamma-glutamate carboxypeptidase) (Folypoly-gamma-glutamate carboxypeptidase) (FGCP) (Folate hydrolase 1) (Prostate-specific membrane antigen) (PSMA) (PSM)	228 3E-59
			A56881	prostate-specific membrane antigen	228 3E-59
			AAA60209.1	prostate-specific membrane antigen	228 3E-59
			AAD51121.1	AF176574 1 folypoly-gamma-glutamate carboxypeptidase	228 3E-59
			AAM34479.1	prostate-specific membrane antigen	228 3E-59
			XP_165392.1	similar to folate hydrolase (prostate-specific membrane antigen) 1; folate hydrolase 1 (prostate-specific membrane antigen)	224 6E-58

**NM 025891**

-1.70

60kDa BRG-1/Brm associated factor subunit c isoform 2

835 0

33

786 0

100	0
745	0

42

623 e-178

020 0-170  
020 0-170

023 E-170  
040 - 177

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504 0 160

601-9460

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541 e-153

450 e-126

340 5e-93

1  
2  
3  
4  
5  
6  
7

0	607
0	752

10 cc/

ATHUSM	actin alpha 2, aortic smooth muscle - human	750	0
NP_001606.1	actin, gamma 2 propeptide; actin, alpha-3	748	0
NP_001605.1	actin, gamma 1 propeptide; actin, cytoplasmic 2; deafness, autosomal dominant 26; deafness, autosomal dominant 20; cytoskeletal gamma-actin	721	0
JC5818	gamma-actin - human	721	0
NP_001092.1	beta actin; beta cytoskeletal actin	720	0
AAH16045.1	Beta actin	718	0
CAA45026.1	mutant beta-actin (beta'-actin)	716	0
AAH08633.1	actin, beta	715	0
AAH17450.1	Unknown (protein for IMAGE:3538275)	701	0
AAH12854.1	ACTB protein	699	0
XP_293924.1	similar to RIKEN cDNA 4732495G21 gene	686	0
XP_371558.2	similar to FKSG30	670	0
XP_065237.5	similar to FKSG30	669	0
AAG50355.1	FKSG30	668	0
XP_372957.1	similar to FKSG30	666	0
XP_292982.4	similar to pote protein; Expressed in prostate, ovary, testis, and placenta	666	0
AAA51586.1	actin prepeptide	650	0
0902248A	actin beta related pseudogene	571 e-162	
AAH23548.1	ACTG1 protein	504 e-142	
AAA51580.1	gamma-actin	443 e-124	
AAH06372.1	ARP1 actin-related protein 1 homolog B, centractin beta	430 e-120	
	ARP1 actin-related protein 1 homolog B, centractin beta; centractin beta; ARP1 (actin-related protein 1, yeast) homolog B (centractin beta); PC3; ARP1, yeast homolog B	430 e-120	
NP_005726.1	ARP1 actin-related protein 1 homolog A, centractin alpha; ARP1 (actin-related protein 1, yeast) homolog A (centractin alpha); centractin alpha; actin-RPV; centrosome-associated actin homolog; ARP1, yeast homolog A	423 e-118	
NP_005727.1			
1818358A	actin-related protein	421 e-117	





NP_005150.1	cardiac muscle alpha actin proprotein; smooth muscle actin	755	0
NP_001606.1	actin, gamma 2 propeptide; actin, alpha-3	754	0
NP_001091.1	alpha 1 actin precursor; alpha skeletal muscle actin	753	0
NP_001605.1	actin, gamma 1 propeptide; actin, cytoplasmic 2; deafness, autosomal dominant 26; deafness, autosomal dominant 20;	724	0
JC5818	gamma-actin	724	0
NP_001092.1	beta actin; beta cytoskeletal actin	724	0
AAH16045.1	Beta actin	722	0
CAA45026.1	mutant beta-actin (beta'-actin)	720	0
AAH08633.1	actin, beta	719	0
AAH12854.1	ACTB protein	703	0
AAH17450.1	Unknown (protein for IMAGE:3538275)	701	0
XP_293924.1	similar to RIKEN cDNA 4732495G21 gene	689	0
XP_371558.2	similar to FKSG30	672	0
XP_065237.5	similar to FKSG30	671	0
AAG50355.1	FKSG30	671	0
XP_292982.4	similar to pote protein; Expressed in prostate, ovary, testis, and placenta	668	0
XP_372957.1	similar to FKSG30	668	0
AAA51586.1	actin prepeptide	661	0
0902248A	actin beta related pseudogene	575 e-163	
AAH23548.1	ACTG1 protein	506 e-143	
AAA51580.1	gamma-actin	445 e-124	
AAH06372.1	ARP1 actin-related protein 1 homolog B, contractin beta	431 e-120	
NP_005726.1	ARP1 actin-related protein 1 homolog B, contractin beta; ARP1 (actin-related protein 1, yeast) homolog B (contractin beta); PC3; ARP1, yeast homolog B	429 e-120	
NP_005727.1	ARP1 actin-related protein 1 homolog A, contractin alpha; ARP1 (actin-related protein 1, yeast) homolog A (contractin alpha); contractin alpha; actin-RPV; centrosome-associated actin homolog; ARP1, yeast homolog	422 e-118	
1818358A	actin-related protein	421 e-117	
ARM1_HUMA			
N	Actin related protein M1	387 e-107	

NP_115876.2	actin related protein M1	382 e-105
AAH07289.1	Actin related protein M1	382 e-105
CAA57692.1	beta-centractin	380 e-105
NP_612146.1	actin-related protein T1	369 e-102
AAM00432.1	actin-related protein T1	369 e-102
NP_536356.3	actin-related protein M2; actin-related protein hArpM2; actin-related protein T2	369 e-102
BAB85862.1	actin-related protein hArpM2	367 e-101
AAP20055.1	HSD27	366 e-101
AAH29499.1	Actin-related protein M2	365 e-100
NP_005713.1	actin-related protein 2; ARP2 (actin-related protein 2, yeast) homolog	356 6e-98
AAH14546.1	Actin-related protein 2	353 5e-97
NP_006678.1	actin-like 7A; actin-like 7-alpha	328 2e-89
XP_208204.1	similar to actin-related protein 2	326 7e-89
XP_377904.1	similar to cytoplasmic beta-actin	325 2e-88
AAP37280.1	actin alpha 1 skeletal muscle protein	323 6e-88
AAH10417.2	ACTG1 protein	323 8e-88
AAH36253.1	ACTR2 protein	318 1e-86
NP_006677.1	actin-like 7B; actin-like 7-beta	316 9e-86
AAH09544.1	Unknown (protein for IMAGE:3897065)	311 2e-84
BAB71690.1	unnamed protein product	303 6e-82
NP_848620.1	actin-like	303 8e-82
AAP20052.1	HSD21	301 2e-81
NM_013456	F:(C-D)	168
NP_038484.1	Mm.5316	5 0
	NP_001095.1	skeletal muscle specific actinin, alpha 3
	NP_001094.1	actinin, alpha 2
	NP_001093.1	actinin, alpha 1
	FAHUAA	alpha-actinin 1 - human
	NP_004915.2	actinin, alpha 4
		144
		9 0
		141
		0 0
		140
		7 0
		134
		8 0

BAA24447.1	alpha actinin 4	134 8	0
AAC17470.1	alpha actinin	125	0
AAH15620.2	ACTN4 protein	5	0
CAA38970.1	alpha-actinin	924	0
CAD62344.1	unnamed protein product	899	0
1HCI_A	Chain A, Crystal Structure Of The Rod Domain Of Alpha-Actinin	869	0
1HCI_B	Chain B, Crystal Structure Of The Rod Domain Of Alpha-Actinin	753	0
XP_293669.4	similar to actinin, alpha 4	753	0
NP_842565.1	spectrin, beta, non-erythrocytic 1 isoform 2; Spectrin, beta, nonerythrocytic-1 (beta-fodrin)	497 e-140	
NP_003119.1	spectrin, beta, non-erythrocytic 1 isoform 1; Spectrin, beta, nonerythrocytic-1 (beta-fodrin)	426 e-118	
NP_008877.1	spectrin, beta, non-erythrocytic 2	426 e-118	
AAA60578.1	spectrin Rouen (beta-220-218) mutant coding sequence	415 e-115	
NP_000338.2	spectrin, beta, erythrocytic (includes spherocytosis, clinical type I); Spectrin, beta, erythrocytic; spectrin, beta, erythrocytic (includes spherocytosis, clinical type I)	405 e-112	
SPCB_HUMA N	Spectrin beta chain, erythrocyte (Beta-I spectrin)	405 e-112	
AAQ14859.1	beta spectrin IV	405 e-112	
AAG42473.1	spectrin beta IV	399 e-110	
NP_066022.1	spectrin, beta, non-erythrocytic 4	399 e-110	
SPCQ_HUMA N	Spectrin beta chain, brain 3 (Spectrin, non-erythroid beta chain 3)(Beta-IV spectrin)	399 e-110	
NP_079489.1	spectrin, beta, non-erythrocytic 4	399 e-110	
AAF93171.1	betaIV spectrin isoform sigma2	396 e-110	

AAF93173.1	betaIV spectrin isoform sigma4	394 e-109
1QUU_A	Chain A, Crystal Structure Of Two Central Spectrin-Like Repeats From Alpha-Actinin	379 e-104
NP_057726.1	spectrin, beta, non-erythrocytic 5; beta V spectrin	344 5e-94
AAB41498.1	alpha II spectrin	264 7e-70
AAH53521.1	SPTAN1 protein	264 7e-70
NP_003118.1	spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	259 2e-68
NP_000436.2	plectin 1 isoform 1; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	245 3e-64
G02520	plectin - human	245 3e-64
NP_958782.1	plectin 1 isoform 6; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	245 3e-64
NP_958785.1	plectin 1 isoform 10; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	245 3e-64
NP_958784.1	plectin 1 isoform 8; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	245 3e-64
NP_958786.1	plectin 1 isoform 11; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	245 3e-64
NP_958781.1	plectin 1 isoform 3; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	245 3e-64
NP_958780.1	plectin 1 isoform 2; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	245 3e-64
NP_958783.1	plectin 1 isoform 7; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	245 3e-64
PLE1_HUMA	Plectin 1 (PLTN) (PCN) (Hemidesmosomal protein 1) (HD1)	241 4e-63
I39160	dystonin isoform 1 - human (fragment)	231 4e-60
BPA1_HUMA	Bullous pemphigoid antigen 1 isoforms 1/2/3/4/5/8 (230 kDa bullous pemphigoid antigen) (BPA) (Hemidesmosomal plaque protein)(Dystonia musculorum protein)	231 4e-60
NP_899236.1	bullous pemphigoid antigen 1 isoform 1; bullous pemphigoid antigen 1 (230/240kD); dystonin; hemidesmosomal plaque protein	231 4e-60
MACF_HUMA	Microtubule-actin crosslinking factor 1, isoforms 1/2/3 (Actin cross-linking family protein 7) (Macrophilin 1) (Trabeculin-alpha) (620 kDa actin-binding protein)	224 8e-58

BAA83821.1		actin binding protein ABP620	224 8e-58
NP_036222.3		microfilament and actin filament cross-linker protein isoform a; 620 kDa actin binding protein; actin cross-linking factor; macrophin 1; trabeculin-alpha; actin cross-linking family protein 7	224 8e-58
AAF06360.1		trabeculin-alpha	223 2e-57
S66292		actin-crosslinking protein ACF7 - human (fragment)	215 3e-55
1MB8_A		Chain A, Crystal Structure Of The Actin Binding Domain Of Plectin	211 7e-54
CAA60503.1		alpha-spectrin	203 1e-51
NM_026369	F:(C-D)		
NP_080645.1	Mm.288974 -1.38	actin related protein 2/3 complex subunit 5; Arp2/3 protein complex subunit p16	293 8e-79
AAH57237.1		ARPC5 protein	285 1e-76
AAP97155.1		ARC16-2	211 4e-54
NP_112240.1		actin related protein 2/3 complex, subunit 5-like	210 5e-54
NM_018817	F:(C-D)	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin a-like	121
NP_061287.1	Mm.274232 -1.37	1; HepA-related protein; SMARCA-like protein 1	3 0
AAH16482.1		SWI/SNF-related matrix-associated actin-dependent regulator of chromatin a-like	121
		1	0 0
AAF24984.1		HepA-related protein HARP	120
			5 0
T34557		hypothetical protein DKFZp434B1050.1 - human (fragment)	112
BAA90955.1		unnamed protein product	5 0
BAC04536.1		unnamed protein product	975 0
NM_026552	F:(C-D)		220 1e-56
NP_080828.1	Mm.289306 -1.35	actin related protein 2/3 complex subunit 4; Arp2/3 protein complex subunit p20	326 5e-89
AAH12596.2		ARPC4 protein	322 1e-87
AF316037	F:(C-D)	actin-binding LIM protein 1 isoform a; LIM actin-binding protein 1; limatin;	130
NP_848803.2	Mm.244618 -1.35	actin-binding LIM protein	7 0
AAC51676.1		actin-binding double-zinc-finger protein	130
			5 0
BAA06681.2		KIAA0059	127
			2 0

NM_019785 NP_062759.1 Mm.29317	F:(C-D) -1.32	NP_006710.2	actin-binding LIM protein 1 isoform m; LIM actin-binding protein 1; limatin; actin-binding LIM protein	111 3	0
		NP_006711.2	actin-binding LIM protein 1 isoform s; LIM actin-binding protein 1; limatin; actin-binding LIM protein	756	0
		BAA74866.2	KIAA0843 protein	651	0
		NP_055760.1	actin binding LIM protein family, member 3	651	0
		AAH67214.1	Unknown (protein for IMAGE:6188753)	518 e-146	
		BAB47437.1	KIAA1808 protein	508 e-143	
		NP_115808.2	actin binding LIM protein family, member 2	506 e-143	
		BAC04414.1	unnamed protein product	501 e-141	
		AAH02448.1	ABLIM1 protein	433 e-121	
		AAH01665.1	ABLIM3 protein	401 e-111	
NM_016860 NP_058556.1 Mm.3118	F:(C-D) -1.31	NP_060947.1	uncharacterized hypothalamus protein HARP11	813	0
		BAA91243.1	unnamed protein product	813	0
		BAB14083.1	unnamed protein product	811	0
		CAD62610.1	unnamed protein product	561 e-160	
		CAD61940.1	unnamed protein product	430 e-120	
			ARP1 actin-related protein 1 homolog A, centractin alpha; ARP1 (actin-related protein 1, yeast) homolog A (centractin alpha); centractin alpha; actin-RPV; centrosome-associated actin homolog; ARP1, yeast homolog	755	0
		1818358A	actin-related protein	753	0
			ARP1 actin-related protein 1 homolog B, centractin beta; centractin beta; ARP1 (actin-related protein 1, yeast) homolog B (centractin beta); PC3; ARP1, yeast homolog B	709	0
		NP_005726.1	ARP1 actin-related protein 1 homolog B, centractin beta	708	0
		CAA57692.1	beta-centractin	616 e-176	
NP_001605.1 JC5818			actin, gamma 1 propeptide; actin, cytoplasmic 2; deafness, autosomal dominant 26; deafness, autosomal dominant 20;	425 e-118	
		NP_005150.1	cardiac muscle alpha actin proprotein; smooth muscle actin	425 e-118	
		NP_001092.1	beta actin; beta cytoskeletal actin	425 e-118	
				424 e-118	

AAH08633.1	actin, beta	424 e-118
AAH16045.1	Beta actin	424 e-118
CAA45026.1	mutant beta-actin (beta'-actin)	423 e-118
NP_001091.1	alpha 1 actin precursor; alpha skeletal muscle actin	423 e-118
NP_001604.1	alpha 2 actin; alpha-cardiac actin	422 e-117
NP_001606.1	actin, gamma 2 propeptide; actin, alpha-3	422 e-117
ATHUSM	actin alpha 2; aortic smooth muscle	422 e-117
XP_293924.1	similar to RIKEN cDNA 4732495G21 gene	417 e-116
AAH17450.1	Unknown (protein for IMAGE:3538275)	410 e-114
AAH12854.1	ACTB protein	408 e-113
AAG50355.1	FKSG30	408 e-113
XP_065237.5	similar to FKSG30	408 e-113
XP_371558.2	similar to FKSG30	404 e-112
XP_292982.4	similar to pote protein; Expressed in prostate, ovary, testis, and placenta	404 e-112
XP_372957.1	similar to FKSG30	404 e-112
AAA51586.1	actin prepeptide	355 2e-97
0902248A	actin beta related pseudogene	330 6e-90
NP_005713.1	actin-related protein 2; ARP2 (actin-related protein 2, yeast) homolog	322 2e-87
AAH14546.1	Actin-related protein 2	318 2e-86
NP_115876.2	actin related protein M1	314 6e-85
ARM1_HUMA	Actin related protein M1	314 6e-85
NP_536356.3	actin-related protein M2; actin-related protein hArpM2; actin-related protein T2	309 1e-83
AAH07289.1	Actin related protein M1	309 2e-83
BAB85862.1	actin-related protein hArpM2	308 2e-83
AAH29499.1	Actin-related protein M2	307 7e-83
AAH23548.1	ACTG1 protein	297 6e-80
XP_208204.1	similar to actin-related protein 2	296 1e-79
NP_612146.1	actin-related protein T1	295 4e-79

AAM00432.1	actin-related protein T1	295 4e-79
AAP20055.1	HSD27	291 4e-78
AAH36253.1	ACTR2 protein	287 8e-77
NP_006678.1	actin-like 7A; actin-like 7-alpha	267 6e-71
NP_006677.1	actin-like 7B; actin-like 7-beta	260 1e-68
AA51580.1	gamma-actin	253 9e-67
BAB71690.1	unnamed protein product	248 4e-65
NP_848620.1	actin-like	247 7e-65
AAP20052.1	HSD21	246 2e-64
NP_065178.1	actin-related protein 3-beta; actin-related protein 3-beta; actin-related protein Arp11; actin-related protein Arp11	235 3e-61
NP_005712.1	ARP3 actin-related protein 3 homolog; ARP3 (actin-related protein 3, yeast) homolog	235 3e-61
NP_057272.1	BAF53b; actin-related protein; hArpN alpha	213 1e-54
CAB66543.1	hypothetical protein	203 1e-51
NM_020618	F:(C-D)	
NP_065643.1	Mm.27330 -1.30 NP_003070.3 SWI/SNF-related matrix-associated actin-dependent regulator of chromatin e1; mammalian chromatin remodeling complex BRG1-associated factor 57	597 e-170
NM_011779	F:(C-D)	
NP_035909.2	Mm.320560 -1.30 T47172 SWI/SNF-related matrix-associated actin-dependent regulator of chromatin e1	594 e-169
NP_055140.1	hypothetical protein DKFZp762H186.1 - human (fragment)	954 0
NP_065174.1	coronin, actin-binding protein, 1C; coronin, actin-binding protein, 1C; coronin 1C	946 0
NP_009005.1	coronin, actin-binding protein, 1B	758 0
AAA77058.1	coronin, actin binding protein, 1A; coronin, actin-binding, 1A; coronin, actin-binding protein, 1A; coronin-1	648 0
BAA76769.1	coronin-like protein	644 0
NP_006082.1	KIAA0925 protein	412 e-114
CO2B_HUMA	coronin, actin binding protein, 2B; clipin C; coronin, actin-binding, 2B; coronin, actin-binding protein, 2B	411 e-114
N	Coronin 2B (Coronin-like protein C) (ClipinC) (Protein FC96)	409 e-113



NP_438171.1	coronin, actin binding protein, 2A; coronin, actin-binding protein, 2A; coronin 2A; coronin-like protein B; WD-repeat protein 2; WD protein IR10	408 e-113
NP_003380.2	coronin, actin binding protein, 2A; coronin, actin-binding protein, 2A; coronin 2A; coronin-like protein B; WD-repeat protein2; WD protein IR10	408 e-113
AAB47807.1	WD protein IR10	404 e-112
T47174	hypothetical protein DKFZp762l166.1 - human (fragment)	389 e-107
AAS48630.1	unknown	314 7e-85
NP_116243.1	hypothetical protein FLJ14871	311 5e-84
AAQ04659.1	Unknown	311 6e-84
NP_078811.1	hypothetical protein FLJ22021	234 6e-61
NM_033268	F:(C-D)	171
NP_150371.2	Mm.195067 -1.29	2 0
NP_001094.1	actinin, alpha 2	141
NP_001095.1	skeletal muscle specific actinin, alpha 3	2 0
NP_001093.1	actinin, alpha 1	139
FAHUAA	alpha-actinin 1 - human	4 0
NP_004915.2	actinin, alpha 4	139
BAA24447.1	alpha actinin 4	1 0
AAC17470.1	alpha actinin	136
AAH15620.2	ACTN4 protein	1 0
1HCL_A	Chain A, Crystal Structure Of The Rod Domain Of Alpha-Actinin	126
1HCL_B	Chain B, Crystal Structure Of The Rod Domain Of Alpha-Actinin	5
CAA38970.1	alpha-actinin	941 0
CAD62344.1	unnamed protein product	891 0
XP_293669.4	similar to actinin, alpha 4	887 0
		835 0
		524 e-148

1QUU_A	Chain A, Crystal Structure Of Two Central Spectrin-Like Repeats From Alpha-Actinin	455 e-127
NP_008877.1	spectrin, beta, non-erythrocytic 2	412 e-114
NP_842565.1	spectrin, beta, non-erythrocytic 1 isoform 2; Spectrin, beta, nonerythrocytic-1 (beta-fodrin)	408 e-113
NP_003119.1	spectrin, beta, non-erythrocytic 1 isoform 1; Spectrin, beta, nonerythrocytic-1 (beta-fodrin)	407 e-113
NP_000338.2	spectrin, beta, erythrocytic (includes spherocytosis, clinical type I); Spectrin, beta, erythrocytic; spectrin, beta, erythrocytic (includes sperocytosis, clinical type I)	391 e-108
SPCB_HUMA N	Spectrin beta chain, erythrocyte (Beta-I spectrin)	391 e-108
AAA60578.1	spectrin Rouen (beta-220-218) mutant coding sequence	391 e-108
AAG42473.1	spectrin beta IV	381 e-105
NP_066022.1	spectrin, beta, non-erythrocytic 4	381 e-105
SPCQ_HUMA N	Spectrin beta chain, brain 3 (Spectrin, non-erythroid beta chain 3)(Beta-IV spectrin)	381 e-105
AAQ14859.1	beta spectrin IV	381 e-105
NP_079489.1	spectrin, beta, non-erythrocytic 4	375 e-103
AAF93171.1	betaIV spectrin isoform sigma2	375 e-103
AAF93173.1	betaIV spectrin isoform sigma4	373 e-103
NP_057726.1	spectrin, beta, non-erythrocytic 5; beta V spectrin	322 2e-87
AAB41498.1	alpha II spectrin	284 5e-76
AAH53521.1	SPTAN1 protein	284 5e-76
NP_003118.1	spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	279 2e-74
CAA60503.1	alpha-spectrin	231 5e-60

NP_958780.1	plectin 1 isoform 2; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	224 6e-58
NP_958784.1	plectin 1 isoform 8; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	224 8e-58
NP_958786.1	plectin 1 isoform 11; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	223 1e-57
NP_958782.1	plectin 1 isoform 6; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	223 1e-57
NP_958785.1	plectin 1 isoform 10; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	223 1e-57
NP_958783.1	plectin 1 isoform 7; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	223 1e-57
NP_000436.2	plectin 1 isoform 1; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	223 1e-57
G02520	plectin - human	223 1e-57
NP_958781.1	plectin 1 isoform 3; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 (Ogna)	223 1e-57
NP_899236.1	bullous pemphigoid antigen 1 isoform 1; bullous pemphigoid antigen 1 (230/240kD); dystonin; hemidesmosomal plaque protein	222 2e-57
I39160	dystonin isoform 1 - human (fragment)	222 2e-57
PLE1_HUMA		
N	Plectin 1 (PLTN) (PCN) (Hemidesmosomal protein 1) (HD1)	220 1e-56
BPA1_HUMA	Bullous pemphigoid antigen 1 isoforms 1/2/3/4/5/8 (230 kDa bullous pemphigoid antigen) (BPA) (Hemidesmosomal plaque protein) (Dystonia musculorum protein)	219 2e-56
N	Microtubule-actin crosslinking factor 1, isoforms 1/2/3 (Actin cross-linking family protein 7) (Macrophilin 1) (Trabeculin-alpha) (620 kDa actin-binding protein) (ABP620)	
MACF_HUMA		
N	actin binding protein ABP620	213 1e-54
BAA83821.1	microfilament and actin filament cross-linker protein isoform a; 620 kDa actin binding protein; actin cross-linking factor; macrophilin 1; trabeculin-alpha; actin cross-linking family protein 7	213 1e-54
NP_036222.3		
AAF06360.1	trabeculin-alpha	213 1e-54
		211 7e-54

SPCA_HUMA			
AA118546	N	Spectrin alpha chain, erythrocyte (Erythroid alpha-spectrin)	210 1e-53
NP_076224	S66292	actin-crosslinking protein ACF7 - human (fragment)	209 2e-53
	F:(C-D)	ARP3 actin-related protein 3 homolog; ARP3 (actin-related protein 3, yeast)	
	Mm.183102 -1.23	NP_005712.1 homolog	850 0
		actin-related protein 3-beta; actin-related protein 3-beta; actin-related protein	
	NP_065178.1	Arp11; actin-related protein Arp11	793 0
	AAP97150.1	actin related protein ARP4	662 0
	AAH15207.1	ARP3BETA protein	597 e-170
	XP_374583.1	similar to actin-related protein Arp11	348 3e-95
	JC7580	actin-related protein Arp11 - human	344 4e-94
	AAK31778.1	FKSG74	253 8e-67
	AAK31776.1	FKSG72	252 2e-66
	AAK31777.1	FKSG73	249 2e-65
	AAH16045.1	Beta actin	248 3e-65
	NP_001092.1	beta actin; beta cytoskeletal actin	248 3e-65
	NP_001605.1	actin, gamma 1 propeptide; actin, cytoplasmic 2; deafness, autosomal dominant 26; deafness, autosomal dominant 20; cytoskeletal gamma-actin	248 4e-65
	JC5818	gamma-actin - human	248 4e-65
	NP_001091.1	alpha 1 actin precursor; alpha skeletal muscle actin	248 5e-65
	CAA45026.1	mutant beta-actin (beta'-actin)	247 6e-65
	AAH08633.1	actin, beta	247 8e-65
	NP_005150.1	cardiac muscle alpha actin proprotein; smooth muscle actin	247 8e-65
	XP_293924.1	similar to RIKEN cDNA 4732495G21 gene	246 1e-64
	ATHUSM	actin alpha 2, aortic smooth muscle - human	246 1e-64
	NP_001604.1	alpha 2 actin; alpha-cardiac actin	246 2e-64
	NP_001606.1	actin, gamma 2 propeptide; actin, alpha-3	245 3e-64
	AAH17450.1	unknown (protein for IMAGE:3538275)	239 2e-62
		ARP1 actin-related protein 1 homolog B, centractin beta; centractin beta; ARP1 (actin-related protein 1, yeast) homolog B (centractin beta); PC3; ARP1, yeast	
	NP_005726.1	homolog B	236 1e-61

AAH12854.1	ACTB protein				236 2e-61
NP_005727.1	ARP1 actin-related protein 1 homolog A, centractin alpha; ARP1 (actin-related protein 1, yeast) homolog A (centractin alpha); centractin alpha; actin-RPV;				235 3e-61
1818358A	actin-related protein				234 4e-61
AAH06372.1	ARP1 actin-related protein 1 homolog B, centractin beta				234 4e-61
XP_372957.1	similar to FKSG30				223 1e-57
XP_065237.5	similar to FKSG30				223 1e-57
AAG50355.1	FKSG30				223 1e-57
XP_292982.4	similar to pote protein; Expressed in prostate, ovary, testis, and placenta				223 1e-57
XP_371558.2	similar to FKSG30				223 2e-57
AAA51586.1	actin prepeptide				211 5e-54
CAA57692.1	beta-centractin				211 6e-54
AAH14546.1	Actin-related protein 2				203 1e-51
NP_005713.1	actin-related protein 2; ARP2 (actin-related protein 2, yeast) homolog				203 1e-51
NM_031878	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d2;				
NP_114084.1	Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60B;				
	Swp73-like protein; chromatin remodeling complex BAF60B subunit; SWI/SNF				
F:(C-D)					
-1.21					
Mm.21772					
NP_003068.2	complex 60 kDa subunit B				828 0
AAC50696.1	SWI/SNF complex 60 kDa subunit				745 0
	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d3;				
	Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60C;				
	Swp73-like protein; chromatin remodeling complex BAF60C subunit; SWI/SNF				
NP_003069.2	complex 60 kDa subunit C				622 e-178
AAR88510.1	60kDa BRG-1/Brm associated factor subunit c isoform 2				619 e-177
AAC50697.1	SWI/SNF complex 60 kDa subunit				596 e-170
AAH09368.2	SMARCD1 protein				589 e-168

			SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d1 isoform a; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60A; chromatin remodeling complex BAF60A subunit; Swp73-like protein; SWI/SNF complex 60 kDa subunit A	589 e-168
NP_003067.2				
AAD23390.1			SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin D1 isoform b; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60A; chromatin remodeling complex BAF60A subunit; Swp73-like protein; SWI/SNF complex 60 kDa subunit A	582 e-165
NP_620710.1				505 e-142
AAC50695.1			SWI/SNF complex 60 KDa subunit	505 e-142
AAS02031.1			unknown	366 e-100
AAS00380.1			unknown	261 5e-69
AAH18953.2			SMARCD2 protein	159 2e-38
AAF20280.1			PRO2451	152 2e-36
NM_019767	F:(C-D)		actin related protein 2/3 complex subunit 1A; actin binding protein	
NP_062741.1	-1.18	Mm.34695	(Schizosaccharomyces pombe sop2-like); SOP2-like protein	730 0
AR1A_HUMA				
N			Actin-related protein 2/3 complex subunit 1A (SOP2-like protein)	723 0
NP_005711.1			actin related protein 2/3 complex subunit 1B; ARP2/3 protein complex subunit p41; actin related protein 2/3 complex, subunit 1A (41 kD)	533 e-151
AAS00381.1			unknown	357 2e-98
NM_011418	F:(C-D)		SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1; sucrose nonfermenting, yeast, homolog-like 1; integrase	
NP_035548.1	-1.14	Mm.279751	interactor 1	754 0
SNF5_HUMA			SWI/SNF related, matrix associated, actin dependent regulator of chromatin subfamily B member 1 (Integrase interactor 1 protein) (hSNF5) (BAF47)	
N				749 0
CAA09759.1			Ini1b	728 0
BAB14784.1			unnamed protein product	710 0
CAA76639.1			SNF5/INI1 protein	685 0



Subtable 1B: Wholly Unfavorable Genes and Proteins

Mouse Gene Protein	Unigene	Behavior	Human Proteins	Human Protein Name	Score (bits)	E-value
NM_007588						
NP_031614.1	Mm.4642	U:(IR-D) 3.8	AAC50300.1	calcitonin receptor	758	0
			BAA86929.1	calcitonin receptor	758	0
			BAA86928.1	calcitonin receptor	758	0
			NP_001733.1	calcitonin receptor	754	0
			I37217	calcitonin receptor	754	0
			CAA49541.1	human calcitonin receptor	754	0
			CAA57849.1	truncated isomer of calcitonin receptor	754	0
			AAB83945.1	Calcitonin Receptor, alternatively spliced form	754	0
			P30988	CALR_HUMAN Calcitonin receptor precursor (CT-R)	748	0
			S34486	calcitonin receptor	748	0
			AAA35640.1	calcitonin receptor	748	0
			AAB83944.1	Calcitonin Receptor, alternatively spliced form	744	0
			AAC50301.1	calcitonin receptor isoform	731	0
			NP_005786.1	calcitonin receptor-like	511	e-144
			Q16602	CGRR_HUMAN Calcitonin gene-related peptide type 1 receptor precursor (CGRP type 1 receptor)	511	e-144
			JC2477	calcitonin receptor-like protein	511	e-144
			AAA62158.1	calcitonin-like receptor	511	e-144
			AAC41994.1	CGRP type 1 receptor	511	e-144
			NP_000307.1	parathyroid hormone receptor 1	237	1e-61
			Q03431	PTRR_HUMAN Parathyroid hormone/parathyroid hormone-related peptide receptor precursor (PTH/PTHr receptor)	237	1e-61
			A49191	parathyroid hormone/PTH-related peptide receptor	237	1e-61



				AAA36525.1	parathyroid hormone receptor	237	1e-61
				CAA48589.1	parathyroid hormone receptor	237	1e-61
				AAA56774.1	parathyroid hormone/parathyroid hormone related peptide receptor	237	1e-61
				AAB60657.1	parathyroid hormone/PTH-related peptide receptor	237	1e-61
				2119172A	parathyrin receptor	237	1e-61
				Q13324	CRF2_HUMAN Corticotropin releasing factor receptor 2 precursor (CRF-R 2) (CRF2) (Corticotropin-releasing hormone receptor 2) (CRH-R 2)	221	6e-57
				AAC71653.1	corticotropin-releasing factor receptor	221	6e-57
				BAC05922.1	seven transmembrane helix receptor	221	6e-57
				AAB94503.1	corticotropin releasing hormone receptor type 2 beta isoform	221	8e-57
				AAB94562.1	corticotropin releasing hormone receptor type 2 gamma isoform; CRH type 2 gamma receptor	220	1e-56
				AAC71654.1	corticotropin releasing hormone receptor type 2 gamma isoform; match to AF019381 (PID:g2738889)	220	1e-56
AK007657							
BAB25167.1	Mm.45138	U:(IR-D) 3.55	NP 115744.2		leucine zipper and CTNNBIP1 domain containing	305	9e-83
			BAB72100.1		Leucine zipper & ICAT homologous protein LZIC	305	9e-83
AK007999							
BAB25399.1	Mm.35718	U:(IR-D) 3.3	XP 114275.1		similar to RIKEN cDNA 2010001C09	244	1e-64
AF282730							
AAF97239.1	Mm.36851	U:(IR-D) 2.78	NP 003247.1		tissue inhibitor of metalloproteinase 4 precursor	409	e-114
			Q99727		TIM4_HUMAN Metalloproteinase inhibitor 4 precursor (TIMP-4) (Tissue inhibitor of metalloproteinases-4)	409	e-114
			AAB40391.1		tissue inhibitor of metalloproteinase 4	409	e-114
			AAC34422.1		tissue inhibitor of metalloproteinase 4	409	e-114
			AAH10553.1		AAH10553 tissue inhibitor of metalloproteinase 4	409	e-114
			NP_003246.1		tissue inhibitor of metalloproteinase 2 precursor	216	3e-56

			P16035	TIM2_HUMAN Metalloproteinase inhibitor 2 precursor (TIMP-2) (Tissue inhibitor of metalloproteinases-2) (CSC-21K)	216	3e-56
			A37128	metalloproteinase inhibitor 2 precursor	216	3e-56
			AAB19474.1	tissue inhibitor of metalloproteinase 2; TIMP-2	216	3e-56
			AAA59581.1	metalloproteinase inhibitor precursor	216	3e-56
			AAA61186.1	metalloproteinase-2 inhibitor precursor	216	3e-56
			AAC50729.1	tissue inhibitor of metalloproteinases-2	216	3e-56
			IGXD	C Chain C, Prommp-2TIMP-2 Complex	214	1e-55
			IGXD	D Chain D, Prommp-2TIMP-2 Complex	214	1e-55
			1BR9	Human Tissue Inhibitor Of Metalloproteinase-2	214	1e-55
			AAB24785.1	TIMP-2, CSC-21K=tissue inhibitor of metalloproteinase	211	9e-55
			AAA21815.1	metalloproteinase-3 tissue inhibitor	200	3e-51
			NP_000353.1	tissue inhibitor of metalloproteinase 3; Tissue inhibitor of metalloproteinase-3, K222 expressed in degenerative retinas	199	4e-51
			P35625	TIM3_HUMAN Metalloproteinase inhibitor 3 precursor (TIMP-3) (Tissue inhibitor of metalloproteinases-3) (MIG-5 protein)	199	4e-51
			S45317	metalloproteinase inhibitor 3 precursor	199	4e-51
			AAA17672.1	tissue inhibitor of metalloproteinase-3 precursor	199	4e-51
			CAA53813.1	tissue inhibitor of metalloproteinases-3	199	4e-51
			AAB60373.1	tissue inhibitor of metalloproteinases-3	199	4e-51
			AAB34532.1	TIMP-3	199	4e-51
			AAC50393.1	tissue inhibitor of metalloproteinases-3	199	4e-51
			AAB07547.1	tissue inhibitor of metalloproteinase-3	199	4e-51
			AAH14277.1	AAH14277 Similar to tissue inhibitor of metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory)	199	4e-51
			CAA38400.1	Tissue inhibitor of metalloproteinases, Type-2	199	6e-51
NM_008302						
NP_032328.1	Min.2180	U:(IR-D) 2.71	NP_031381.2	heat shock 90kDa protein 1, beta; heat shock 90kD protein 1, beta; Heat-shock 90kD protein-1, beta	1202	0

			P08238	HS9B HUMAN Heat shock protein HSP 90-beta (HSP 84) (HSP 90)	1202	0
			AAA36026.1	90 kD heat shock protein	1202	0
			AAH04928.1	Unknown (protein for MGC:10493)	1202	0
			AAH12807.1	Unknown (protein for MGC:3483)	1202	0
			AAH14485.1	Unknown (protein for MGC:23206)	1202	0
			AAH16753.1	Unknown (protein for MGC:1138)	1202	0
			HHHU84	heat shock protein 90-beta [validated]	1197	0
			AAA36025.1	90kDa heat shock protein	1197	0
			1307197A	heat shock protein 90k	1197	0
			T46243	hypothetical protein DKFZp761K0511.1	1170	0
			CAB66478.1	hypothetical protein	1170	0
			NP_005339.1	heat shock 90kDa protein 1, alpha; heat shock 90kD protein 1, alpha	1099	0
			HHHU86	heat shock protein 90-alpha	1099	0
			AAA63194.1	heat shock protein	1099	0
			AAF82792.1	AF275719 i chaperone protein HSP90 beta	1052	0
			AAH09206.1	AAH09206 heat shock 90kD protein 1, beta	1052	0
			AAH23006.1	Unknown (protein for MGC:30059)	961	0
			AAH00987.1	AAH00987 Unknown (protein for IMAGE:3446372)	800	0
			AAC25497.1	Hsp89-alpha-delta-N	750	0
			AAH07989.1	AAH07989 Similar to heat shock 90kD protein 1, alpha	696	0
NM_009056				regulatory factor X2, isoform b; trans-acting regulatory factor 2; DNA binding protein RFX2; HLA class II regulatory factor RFX2	1166	0
NP_033082.1	Mm.102	U:(IR-D) 2.63	NP_602309.1	RFX2 HUMAN DNA-binding protein RFX2	1153	0
			P48378	DNA binding protein RFX2	1153	0
			B55926	DNA binding protein RFX2	1153	0
			CAA53705.1	DNA binding protein RFX2	1153	0
			NP_000626.2	regulatory factor X2, isoform a; trans-acting regulatory factor 2; DNA binding protein RFX2; HLA class II regulatory factor RFX2	1152	0

			AAH28579.1	regulatory factor X <sub>2</sub> 2 (influences HLA class II expression)	1151	0
			NP_602304.1	regulatory factor X3 isoform b; DNA binding protein RFX3	773	0
			AAH22191.1	AAH22191 Unknown (protein for MGC:3664)	773	0
			NP_002910.1	regulatory factor X3 isoform a; DNA binding protein RFX3	751	0
			P48380	RFX3 HUMAN DNA-binding protein RFX3	751	0
			D55926	DNA binding protein RFX3	751	0
			CAA53706.1	DNA binding protein RFX3	751	0
			P22670	RFX1_HUMAN MHC class II regulatory factor RFX1 (RFX) (Enhancer factor C) (EF-C)	686	0
			A35913	regulatory factor X	686	0
			CAA41730.1	MHC class II regulatory factor RFX	686	0
			NP_002909.2	regulatory factor X1; trans-acting regulatory factor 1; enhancer factor C, MHC class II regulatory factor RFX	686	0
			CAC88163.1	bA32F11.1.2 (regulatory factor X <sub>3</sub> 3 (influences HLA class II expression), putative isoform 2)	507	e-143
			CAC88164.1	bA32F11.1.1 (regulatory factor X <sub>3</sub> 3 (influences HLA class II expression), isoform 1)	486	e-136
NM_026346 NP_080622.1	Mm.4046 6	U:(IR-D) 2.28	NP_478136.1	F-box only protein 32 isoform 1; muscle atrophy F-box protein; atrogin-1	710	0
			Q969P5	FX32_HUMAN F-box only protein 32 (Muscle atrophy F-box protein) (MAFbx) (Atrogin-1)	710	0
			AAL16407.1	muscle atrophy F-box protein	710	0
			BAB71333.1	unnamed protein product	710	0
			CAD12251.1	F-box only 32	710	0
			BAB85128.1	F-box domain Fbx25-containing protein	446	e-124
			NP_680482.1	F-box only protein 32 isoform 2; muscle atrophy F-box protein; atrogin-1	422	e-117
			AAH24030.1	similar to RIKEN cDNA 4833442G10 gene	417	e-116
			AAF04526.1	AF174605 1 F-box protein Fbx25	354	4e-97
			NP_036305.1	F-box only protein 25; F-box protein Fbx25	353	6e-97

NM_009244	Mm.19341	U:(IR-D)	AAA51547.1	alpha-1-antitrypsin precursor		508	e-144
NP_033270.1	8	2.26	AAH15642.1	AAH15642 Similar to serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1		508	e-144
			1012287A	antitrypsin alpha1 mutant		507	e-143
			P01009	A1AT_HUMAN Alpha-1-antitrypsin precursor (Alpha-1 protease inhibitor) (Alpha-1-antiproteinase) (PRO0684/PRO2209)		507	e-143
			ITHU	alpha-1-antitrypsin precursor [validated]		507	e-143
			CAA25838.1	alpha 1-antitrypsin		507	e-143
			AAB59375.1	alpha-1-antitrypsin		507	e-143
			AAG35496.1	AF130117 27 PRO2209		507	e-143
			NP_000286.2	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1; Protease inhibitor (alpha-1-antitrypsin); protease inhibitor 1 (anti-elastase), alpha-1-antitrypsin		506	e-143
			AAH11991.1	AAH11991 Similar to serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1		506	e-143
			AAF29581.1	AF113676 1 PRO0684		504	e-142
			AAB59495.1	alpha-1-antitrypsin		504	e-142
			AAA51546.1	alpha-1-antitrypsin		501	e-141
			1HP7	Chain A, A 2.1 Angstrom Structure Of An Uncleaved Alpha-1- Antitrypsin Shows Variability Of The Reactive Center And Other Loops		499	e-141
			1KCT	Alpha1-Antitrypsin		498	e-141
NM_009194							
NP_033220.1	Mm.4168	U:(IR-D)	NP_001037.1	solute carrier family 12 (sodium/potassium/chloride transporters), member 2; Solute carrier family 12 (sodium/potassium/chloride transporters),		1978	0
			P55011	S122_HUMAN Solute carrier family 12 member 2 (Bumetanide-sensitive sodium-(potassium)-chloride cotransporter 1) (Basolateral Na-K-Cl symporter)		1978	0
			A57187	bumetanide-sensitive Na-K-Cl cotransporter		1978	0
			AAC 0561.1	bumetanide-sensitive Na-K-Cl cotransporter		1978	0

				AAH33003.1	Similar to solute carrier family 12 (sodium/potassium/chloride transporters), member 2	1851	0
				NP_000329.1	sodium potassium chloride cotransporter 2; Solute carrier family 12 (sodium/potassium/chloride transporters),	1294	0
				Q13621	S121_HUMAN Solute carrier family 12 member 1 (Bumetanide-sensitive sodium-(potassium)-chloride cotransporter 2) (Kidney-specific Na-K-Cl symporter)	1294	0
				AAB07364.1	bumetanide-sensitive Na-K-2Cl cotransporter	1294	0
				NP_000330.1	solute carrier family 12 (sodium/chloride transporters), member 3; Solute carrier family 12 (sodium/potassium/chloride transporters)	1028	0
				AAC50355.1	thiazide-sensitive Na-Cl	1028	0
				P55017	S123_HUMAN Solute carrier family 12 member 3 (Thiazide-sensitive sodium-chloride cotransporter) (Na-Cl symporter)	1024	0
				G01202	NaCl electroneutral Thiazide-sensitive cotransporter	1021	0
				CAA62613.1	NaCl electroneutral Thiazide-sensitive cotransporter	1021	0
				AAL32454.1	AF439152_1 sodium-potassium-chloride cotransporter	598	e-170
				PC4180	thiazide-sensitive sodium-chloride cotransporter	413	e-114
				AAH40138.1	Similar to solute carrier family 12 (sodium/potassium/chloride	403	e-111
				AAK21008.1	cation-chloride cotransporter-interacting protein 1	261	1e-68
NM_009254							
NP_033280.1	Mm.2623	U:(IR-D) 2.15		NP_004559.2	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6; protease inhibitor 6 (placental thrombin inhibitor)	549	e-156
				P35237	PTI6_HUMAN Placental thrombin inhibitor (Cytoplasmic antiprotease) (CAP)(Protease inhibitor 6) (PI-6)	549	e-156
				AAB30320.1	cytoplasmic antiprotease; CAP	549	e-156
				AAH01394.1	AAH01394 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6	549	e-156
				A48681	placental thrombin inhibitor	548	e-156
				CAA80373.1	thrombin inhibitor	548	e-156
				NP_002631.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8; protease inhibitor 8 (ovalbumin type)	459	e-129

				P50452	SPB8_HUMAN Cytoplasmic antiprotease 2 (CAP2) (CAP-2) (Protease inhibitor 8)(Serpine B8)	459	e-129
				A59273	proteinase inhibitor 8	459	e-129
				AAC41939.1	cytoplasmic antiprotease 2	459	e-129
				NP_004146.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9; protease inhibitor 9 (ovalbumin type)	445	e-125
				P50453	SPB9_HUMAN Cytoplasmic antiprotease 3 (CAP3) (CAP-3) (Protease inhibitor 9)(Serpine B9)	445	e-125
				B59273	proteinase inhibitor 9	445	e-125
				AAC41940.1	cytoplasmic antiprotease 3	445	e-125
				AAC50793.1	serine proteinase inhibitor	445	e-125
				AAH02538.1	AAH02538 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9	445	e-125
				BAB91078.1	serine protease inhibitor 9	445	e-125
				NP_109591.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1; protease inhibitor 2 (anti-elastase), monocyte/neutrophil; protease inhibitor 2 (anti-elastase), monocyte/neutrophil derived	330	3e-90
				P30740	ILEU_HUMAN Leukocyte elastase inhibitor (LEI) (Monocyte/neutrophil elastase inhibitor) (M/NEI) (EI)	330	3e-90
				S27383	elastase inhibitor	330	3e-90
				AAC31394.1	monocyte/neutrophil elastase inhibitor	330	3e-90
				AAH09015.1	AAH09015 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1	330	3e-90
				XP_036951.4	similar to Squamous cell carcinoma antigen 2 (SCCA-2) (Leupin)	327	2e-89
				P48594	SCC2_HUMAN Squamous cell carcinoma antigen 2 (SCCA-2) (Leupin)	327	2e-89
				CAA61420.1	leupin	327	2e-89
				AAA97553.1	squamous cell carcinoma antigen 2	327	2e-89
				AAA92602.1	squamous cell carcinoma antigen	327	2e-89
				BAB21525.1	squamous cell carcinoma antigen 2	327	2e-89
				AAH17401.1	AAH17401 Unknown (protein for MGC:27150)	327	2e-89
				I38202	leupin precursor	327	2e-89

			I38201	squamous cell carcinoma antigen 1	325	7e-89
			NP_008850.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 3; squamous cell carcinoma antigen 1	325	9e-89
			P29508	SCC1_HUMAN Squamous cell carcinoma antigen 1 (SCCA-1) (Protein T4-A)	325	9e-89
			AAA86317.1	squamous cell carcinoma antigen	325	9e-89
			AAA97552.1	squamous cell carcinoma antigen 1	325	9e-89
			AAH05224.1	AAH05224 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 3	325	9e-89
			AAB20405.1	squamous cell carcinoma antigen; SCC antigen	325	9e-89
NM_019431 NP_062304.1	Mm.1037 24	U:(IR-D) 2.09	NP_055220.1	voltage-dependent calcium channel gamma-4 subunit; neuronal voltage-gated calcium channel gamma-4 subunit	540	e-153
			Q9UBN1	CCG4_HUMAN Voltage-dependent calcium channel gamma-4 subunit (Neuronal voltage-gated calcium channel gamma-4 subunit)	540	e-153
			AAF03090.1	calcium channel gamma 4 subunit	540	e-153
			AAF14538.1	AF162692_1 putative voltage-gated calcium channel gamma-4 subunit	540	e-153
			AAH34532.1	calcium channel, voltage-dependent, gamma subunit 4	540	e-153
			NP_006069.1	voltage-dependent calcium channel gamma-2 subunit; stargazin; neuronal voltage-gated calcium channel gamma-2 subunit	303	2e-82
			Q9Y698	CCG2_HUMAN Voltage-dependent calcium channel gamma-2 subunit (Neuronal voltage-gated calcium channel gamma-2 subunit)	303	2e-82
			AAD22738.1	AF096322_1 neuronal voltage-gated calcium channel gamma-2 subunit	303	2e-82
			AAL50049.1	AF361354_1 voltage-dependent calcium channel gamma-8 subunit	302	4e-82
			NP_114101.4	voltage-dependent calcium channel gamma-8 subunit; neuronal voltage-gated calcium channel gamma-8 subunit	300	2e-81
			Q8WXS5	CCG8_HUMAN Voltage-dependent calcium channel gamma-8 subunit (Neuronal voltage-gated calcium channel gamma-8 subunit)	300	2e-81
			AAK20031.1	AF288388_1 calcium channel gamma subunit 8	300	2e-81
			NP_006530.1	voltage-dependent calcium channel gamma-3 subunit; neuronal voltage-gated calcium channel gamma-3 subunit	298	8e-81
			O60359	CCG3_HUMAN Voltage-dependent calcium channel gamma-3 subunit (Neuronal voltage-gated calcium channel gamma-3 subunit)	298	8e-81



				AAC15246.1	Unknown gene product		298	8e-81
				AAD22739.1	AF100346 1 neuronal voltage gated calcium channel gamma-3 subunit		298	8e-81
				AAF42975.1	AF134640 1 calcium channel gamma subunit 3		298	8e-81
				AAH40005.1	calcium channel, voltage-dependent, gamma subunit 3		298	8e-81
				XP_050231.1	similar to calcium channel gamma subunit 8		270	2e-72
				AAK15019.1	AF234892 1 putative voltage gated calcium channel gamma-8 subunit CACNG8			
NM_019999	Mm.1772	U:(IR-D)		NP_072094.1	KIAA1184 protein		659	0
NP_064383.1	72	2.05						
				AAH02937.1	AAH02937 Similar to hypothetical protein MNCb-5687		659	0
				BAA86498.1	KIAA1184 protein		579	e-165
				AAH36457.1	Unknown (protein for MGC:33461)		579	e-165
AK002297	Mm.18130	U:(C-IR)						
BAB21996.1	2	6.3		NP_060464.1	hypothetical protein FLJ10099			
				BAA91444.1	unnamed protein product		620	e-177
				AAH08675.1	hypothetical protein FLJ10099		620	e-177
				AAH12562.1	Similar to hypothetical protein FLJ10099		620	e-177
				AAH10519.1	Similar to hypothetical protein FLJ10099		385	e-106
				NP_478137.1	zinc finger protein 354B		1031	0
NM_013744	Mm.7467	U:(C-IR)						
NP_038772.1	0	6.11						
		U:(IR-D)						
		2.04						
				BAB71556.1	unnamed protein product		1031	0
				AAD05335.1	zinc finger protein EZNF		958	0
				NP_005640.1	transcription factor 17		957	0
				O60765	TC17 HUMAN Transcription factor 17 (Zinc finger protein eZNF)		957	0

				BAA25182.1	HKL1		957	0
				NP_009080.1	zinc finger protein 184 (Kruppel-like)		567	e-161
				AAH22992.1	Unknown (protein for MGC:29879)		567	e-161
				AAC51180.1	kruppel-related zinc finger protein		567	e-161
				XP_166367.1	similar to Zinc finger protein 184		566	e-161
				Q99676	Z184 HUMAN Zinc finger protein 184		566	e-161
				CAA17278.1	b3418.1 (zinc finger protein 184 (Kruppel-like))		566	e-161
				XP_032054.2	similar to EZFIT-related protein 1		536	e-152
				AAK30252.1	AF352026_1 EZFIT-related protein 1		536	e-152
				CAD38551.1	hypothetical protein		536	e-152
				XP_091988.1	similar to zinc finger protein 91 (HPF7, HTF10)		533	e-151
				AAH36110.1	Similar to zinc finger protein 208		531	e-150
NM_018764	Mm.1196	U:(C-IR)		NP_002580.2	protocadherin 7, isoform a precursor; BH-pcdh; BH-protocadherin (brain-heart); brain-heart protocadherin		1856	0
NP_061234.1	4	4.56		O60245	PCH7_HUMAN Protocadherin 7 precursor (Brain-heart protocadherin) (BH-Pcdh)		1855	0
				BAA25194.1	PCDH7 (BH-Pcdh)a		1855	0
				NP_115832.1	protocadherin 7, isoform b precursor; BH-pcdh; brain-heart protocadherin; BH-protocadherin (brain-heart)		1838	0
				T00041	BH-protocadherin PCDH7 (clone BH-Pcdh-b)		1837	0
				BAA25195.1	PCDH7 (BH-Pcdh)b		1837	0
				NP_115833.1	protocadherin 7, isoform c precursor; BH-pcdh; brain-heart protocadherin; BH-protocadherin (brain-heart)		1691	0
				T00042	BH-protocadherin PCDH7 (clone BH-Pcdh-c)		1690	0
				BAA25196.1	PCDH7 (BH-Pcdh)c		1690	0
				NP_115796.1	protocadherin 1, isoform 2 precursor; protocadherin 42; cadherin-like protein 1		817	0
				AAH35812.1	Similar to protocadherin 1 (cadherin-like 1)		816	0
				NP_002578.1	protocadherin 1, isoform 1 precursor; protocadherin 42; cadherin-like protein 1		816	0
				Q08174	PCH1_HUMAN Protocadherin 1 precursor (Protocadherin 42) (PC42) (Cadherin-like protein 1)		816	0

				AAA36419.1	protocadherin 42		816	0
				NP_065136.1	protocadherin 9 precursor; cadherin superfamily protein VR4-11		575	e-163
				AAF89689.2	AF169692_1 protocadherin-9		575	e-163
NM_008121		U:(C-IR) 4.51						
NP_032147.1	Mm.19038 6	U:(C-D) 2.06		NP_005257.2	gap junction protein, alpha 5; 40kDa (connexin 40); gap junction protein, alpha 5, 40kD (connexin 40)		580	e-165
				P36382	CXA5_HUMAN Gap junction alpha-5 protein (Connexin 40) (Cx40)		580	e-165
				AAA91833.1	connexin 40		580	e-165
				AAD37801.1	AF151979_1 connexin 40		580	e-165
				AAA60457.2	connexin40		580	e-165
				AAH13313.1	gap junction protein, alpha 5, 40kD (connexin 40)		580	e-165
				I38429	connexin40		575	e-164
				NP_068773.2	gap junction protein, alpha 3, 46kDa (connexin 46); gap junction protein, alpha 3, 46kD (connexin 46)		301	1e-81
				CAC16957.1	bA264J4.3 (novel connexin (gap junction protein)		301	1e-81
				Q9Y6H8	CXA3_HUMAN Gap junction alpha-3 protein (Connexin 46) (Cx46)		301	1e-81
				AAD42925.1	gap-junction protein alpha 3		301	1e-81
					gap junction protein, alpha 8, 50kDa (connexin 50); gap junction membrane channel protein alpha-8; connexin 50; Gap junction membrane channel protein alpha-8 (connexin 50); gap junction protein, alpha 8, 50kD (connexin 50)		299	4e-81
				NP_005258.1			299	4e-81
				I39176	intrinsic membrane protein MP70		299	4e-81
				AAA77062.1	gap junction membrane channel protein alpha-8		299	4e-81
				P48165	CXA8_HUMAN Gap junction alpha-8 protein (Connexin 50) (Cx50) (Lens fiber protein MP70)		296	3e-80
				AAF32309.1	AF217524_1 gap junction protein alpha 8		296	3e-80
				AAK55516.1	AF271261_1 connexin 58		282	5e-76
				NP_110399.1	connexin 59; gap junction alpha 10		282	5e-76
				P57773	CXAA_HUMAN Gap junction alpha-10 protein (Connexin 59) (Cx59)		282	5e-76

				AAG09406.1	AF179597_1 connexin 59	282	5e-76
				AAD56533.1	AF180815_1 truncated connexin 37 polymorph	270	2e-72
				NP_115991.1	connexin 62	267	2e-71
				AAK51676.1	AF296766_1 connexin 62	267	2e-71
				CAC93847.1	connexin62	267	2e-71
NM_008314		U:(C-IR) 4.49					
NP_032340.1	Mm.4835	U:(C-D) 2.43	I37107		5-HT5A serotonin receptor	584	e-166
			CAA57168.1		5-HT5A serotonin receptor	584	e-166
			AAM21132.1		AF498985_1 5-hydroxytryptamine receptor 5A	584	e-166
			BAA94458.1		5-hydroxytryptamine (serotonin) receptor 1E	212	2e-54
			NP_000856.1		5-hydroxytryptamine (serotonin) receptor 1E	212	2e-54
			P28566		5H1E_HUMAN 5-hydroxytryptamine 1E receptor (5-HT-1E) (Serotonin receptor)	212	2e-54
			A45260		serotonin receptor 1E	212	2e-54
			CAA77558.1		serotonin receptor	212	2e-54
			AAA58353.1		serotonin receptor	212	2e-54
			AAA58355.1		serotonin receptor	212	2e-54
			CAC10582.1		bA76H14.2 (5-hydroxytryptamine (serotonin) receptor 1E)	212	2e-54
			AAM21127.1		AF498980_1 5-hydroxytryptamine receptor 1E	212	2e-54
			NP_000857.1		5-hydroxytryptamine (serotonin) receptor 1F; 5-hydroxytryptamine receptor 1F	209	1e-53
			P30939		5H1F_HUMAN 5-hydroxytryptamine 1F receptor (5-HT-1F) (Serotonin receptor)	209	1e-53
			A47321		serotonin receptor 1F	209	1e-53
			AAA36605.1		serotonin receptor	209	1e-53
			AAA36646.1		serotonin receptor	209	1e-53
			AAM21128.1		AF498981_1 5-hydroxytryptamine receptor 1F	209	1e-53
			BAA90453.1		5-hydroxytryptamine (serotonin) receptor 1F	209	1e-53

				XP_003692.2	similar to 5-hydroxytryptamine 1A receptor (5-HT-1A) (Serotonin receptor) (5-HT1A) (G-21)	205	1e-52
				P08908	5HT1A_HUMAN 5-hydroxytryptamine 1A receptor (5-HT-1A) (Serotonin receptor) (5-HT1A) (G-21)	205	1e-52
				I38209	serotonin receptor 1A	205	1e-52
				CAA40962.1	serotonin 5-HT1a receptor	205	1e-52
				AAA66493.1	serotonin receptor	205	1e-52
				BAA94488.1	serotonin receptor 1A	205	1e-52
				AAM21125.1	AF498978_1 5-hydroxytryptamine receptor 1A	205	1e-52
				XP_092299.1	similar to KIAA0622 protein - human (fragment)	205	1e-52
				NP_000854.1	5-hydroxytryptamine (serotonin) receptor 1B; 5-HT1B; 5-HT1DB	204	2e-52
				P28222	5HT1B_HUMAN 5-hydroxytryptamine 1B receptor (5-HT-1B) (Serotonin receptor)(5-HT-1D-beta) (Serotonin 1D beta receptor) (S12)	204	2e-52
				JN0268	serotonin receptor 1B	204	2e-52
				AAA58675.1	serotonin 1Db receptor	204	2e-52
				AAA36029.1	serotonin receptor	204	2e-52
				AAA36030.1	5-hydroxytryptamine 1D receptor	204	2e-52
				BAA01763.1	serotonin 1B receptor	204	2e-52
				AAA60316.1	serotonin 1D receptor	204	2e-52
				CAB51537.1	dJ501M23.1 (5-hydroxytryptamine (serotonin) receptor 1B)	204	2e-52
				BAA94455.1	5-hydroxytryptamine (serotonin) receptor 1B	204	2e-52
				2209242B	serotonin receptor:ISOTYPE=1D-beta	204	2e-52
				NP_000515.1	5-hydroxytryptamine (serotonin) receptor 1A	202	2e-51
				CAA31908.1	receptor protein (AA 1 - 421)	202	2e-51
				AAA36440.1	guanine nucleotide-binding regulatory protein-coupled recepto	202	2e-51
				1311340A	G protein coupled receptor	202	2e-51



				BAB11985.1	WNT-2B Isoform 2	726	0
					wingless-type MMTV integration site family, member 2B, isoform WNT-2B1; wingless-type MMTV integration site family, member 13; XWNT2, Xenopus, homolog of		
				NP_004176.2		702	0
				BAB11984.1	WNT-2B Isoform 1	702	0
				T09612	secreted glycoprotein Wnt-13	696	0
				CAA96283.1	Wnt-13	696	0
				NP_003382.1	wingless-type MMTV integration site family member 2 precursor; int-1 related protein; oncogene INT1-like 1; secreted growth factor	535	e-152
				P09544	WNT2_HUMAN WNT-2 protein precursor (IRP protein) (Int-1 related protein)	535	e-152
				S00834	int-1-like protein 1 precursor	535	e-152
				CAA30725.1	Irp protein (AA 1-360)	535	e-152
				AAH29854.1	wingless-type MMTV integration site family member 2	535	e-152
				AAB67043.1	secreted growth factor	404	e-112
				NP_003383.1	wingless-type MMTV integration site family, member 5A precursor; proto-oncogene Wnt-5A precursor; WNT-5A protein precursor	360	2e-99
				P41221	WNT5A_HUMAN WNT-5A protein precursor	360	2e-99
				A48914	proto-oncogene Wnt-5A precursor	360	2e-99
				AAA16842.1	hWNT5A	360	2e-99
				NP_116031.1	wingless-type MMTV integration site family, member 5B precursor; WNT-5B protein precursor	358	1e-98
				NP_110402.2	wingless-type MMTV integration site family, member 5B precursor;	358	1e-98
				WNT-5B protein precursor			
				Q9H1J7	WNT5B_HUMAN WNT-5B protein precursor	358	1e-98
				AAH01749.1	AAH01749 Similar to wingless-related MMTV integration site 5B	358	1e-98
				BAB62039.1	WNT5B	358	1e-98
				NP_478679.1	wingless-type MMTV integration site family, member 7B precursor	355	1e-97

				P56706	WN7B_HUMAN WNT-7B protein precursor	355	1e-97
				BAB68399.1	WNT7B	355	1e-97
				AAH34923.1	wingless-type MMTV integration site family, member 7B	355	1e-97
				AAN32640.1	AF416743_1 WNT7B	355	1e-97
				NP_004616.2	wingless-type MMTV integration site family, member 7A precursor; proto-oncogene Wnt7a protein		
				AAH08811.1	Unknown (protein for MGC:10346)	348	1e-95
				AAG38659.1	WNT5b precursor	348	2e-95
AK011231		U:(C-IR) 3.61 U:(C-D) 2.66 U:(IR-D) 2.42					
BAB27481.1	Mm.22533			NP_055330.1	CCR4-NOT transcription complex, subunit 2; NOT2 (negative regulator of transcription 2, yeast) homolog	877	0
				AAF29827.1	AF180473_1 Not2p	877	0
				AAH02597.1	CCR4-NOT transcription complex, subunit 2	877	0
				AAH11826.1	Similar to CCR4-NOT transcription complex, subunit 2	877	0
				BAA91313.1	unnamed protein product	751	0
				AAF29095.1	AF161480_1 HSPC131	729	0
				AAG39297.1	AF113226_1 MSTP046	728	0
				T46494	hypothetical protein DKFZp434M0572.1	326	8e-89
				CAB70869.1	hypothetical protein	326	8e-89
NM_009613		U:(C-IR) 3.6 U:(C-D) 2.86					
NP_033743.1	Mm.89854			NP_002381.2	a disintegrin and metalloprotease domain 11, isoform 1 preproprotein; metalloproteinase-like, disintegrin-like, cysteine-rich protein	1454	0
				BAA32352.1	MDC/ADAM11	1454	0
				O75078	AD11_HUMAN ADAM 11 precursor (A disintegrin and metalloproteinase domain 11) (Metalloproteinase-like, disintegrin-like, and cysteine-rich protein) (MDC)	1451	0
				I65967	disintegrin-like metalloproteinase (EC 3.4.24.-), splice form 2	1345	0



				BAA06670.1	metalloprotease/disintegrin-like protein	1340	0
				NP_067625.1	a disintegrin and metalloprotease domain 11, isoform 2 preproprotein; metalloproteinase-like, disintegrin-like, cysteine-rich protein	1011	0
				S38539	disintegrin-like metalloproteinase (EC 3.4.24.-), splice form 1	1011	0
				AAB29191.1	MDC=metalloprotease/disintegrin-like cysteine-rich protein [human, cerebellum, Peptide, 524 aa]	1011	0
				BAA04213.1	MDC protein	1011	0
				BAA06671.1	metalloprotease/disintegrin-like protein	1008	0
				NP_068367.1	a disintegrin and metalloproteinase domain 22 isoform 5 proprotein; MDC2 delta	825	0
				BAA32350.1	MDC2 beta	825	0
				AAF22476.2	AF073291_1 MDC2	825	0
				NP_057435.2	a disintegrin and metalloproteinase domain 22 isoform 3 proprotein; MDC2 delta	825	0
				NP_068368.2	a disintegrin and metalloproteinase domain 22 isoform 2 proprotein; MDC2 delta	825	0
AK002979			U:(C-IR) 3.58				
BAB22492.1	Mm.19588 1		U:(C-D) 2.07	NP_056537.1	calcyon	336	5e-92
				Q9NYX4	D1IP_HUMAN D1 dopamine receptor-interacting protein calcyon	336	5e-92
				AAF34714.1	AF225903_1 D1 dopamine receptor interacting protein calcyon	336	5e-92
				AAH38978.1	Similar to calcyon; D1 dopamine receptor-interacting protein	336	5e-92
NM_008714			U:(C-IR) 3.55				
NP_032740.1	Mm.31255		U:(C-D) 2.19	P46531	NTC1_HUMAN Neurogenic locus notch homolog protein 1 precursor (Notch 1) (hN1) (Translocation-associated notch protein TAN-1)	4646	0
				AAG33848.1	AF308602_1 NOTCH 1	4646	0
				A40043	notch protein homolog TAN-1 precursor	4528	0
				AAAG0614.1	TANI	4482	0
				NP_077719.2	notch 2 preproprotein	2628	0
				AAG37073.1	AF315356_1 NOTCH2 protein	2627	0

			Q04721	NTC2_HUMAN Neurogenic locus notch homolog protein 2 precursor (Notch 2) (hN2)	2627	0
			AAA36377.2	NOTCH 2	2627	0
			AAC14346.1	Notch3	2065	0
			NP_000426.1	Notch homolog 3	2065	0
			Q9UM47	NTC3_HUMAN Neurogenic locus notch homolog protein 3 precursor (Notch 3)	2065	0
			S78549	notch3 protein	2065	0
			AAB91371.1	Notch3	2065	0
			AAC15789.1	Notch 3	2065	0
			NP_004548.1	Notch homolog 4 (Drosophila); Notch, drosophila, homolog of, 4; Notch (Drosophila) homolog 4	1023	0
			Q99466	NTC4_HUMAN Neurogenic locus notch homolog protein 4 precursor (Notch 4) (hNotch4)	1023	0
			AAC32288.1	Notch4	1023	0
AK012553		U:(C-IR) 3.54				
BAB28313.1	Mm.45628	U:(C-D) 2.46	NP_001575.1	chromosome 11 open reading frame 8; 239FB	627	e-180
			Q15777	239F_HUMAN Fetal brain protein 239	627	e-180
			AAC50564.1	239FB gene product	627	e-180
			AAH31582.1	chromosome 11 open reading frame 8	627	e-180
			212285A	239FB gene	627	e-180
			NP_001576.2	chromosome 22 open reading frame 1; 239AB	518	e-147
			O15442	239A_HUMAN Adult brain protein 239	518	e-147
			AAC51673.2	239AB	518	e-147
			AAH28035.1	Unknown (protein for MGC:40027)	518	e-147
			CAC48257.1	dJ873F21.1 (brain protein 239)	284	2e-76
			CAC10467.1	dJ710M3.1 (chromosome 11 open reading frame 8(Fetal brain protein 239))	253	5e-67



			O00327	BMAL_HUMAN BMAL1 protein (Brain and muscle ARNT-like 1) (Member of PAS protein 3) (Basic-helix-loop-helix-PAS orphan MOP3) (BHLH-PAS protein JAP3)	301	2e-81
			BAA19968.1	BMAL1a	301	2e-81
			NP_001169.2	aryl hydrocarbon receptor nuclear translocator-like	301	2e-81
			AAB37248.1	bHLH-PAS protein JAP3	301	2e-81
			AAC24353.1	basic-helix-loop-helix-PAS orphan MOP3	301	2e-81
			AAC51213.1	PAS protein 3	301	3e-81
			JC5405	brain and muscle Ah receptor nuclear translocator-like protein, BMAL1b	300	5e-81
			BAA19935.1	BMAL1b	300	5e-81
NM_009004		U:(C-IR) 3.26				
NP_033030.1	Mm.19663 8	U:(C-D) 2.41				
			NP_005724.1	RAB6 interacting, kinesin-like (rabkinesin6)	1345	0
			O95235	RB6K_HUMAN Rabkinesin-6 (RAB6-interacting kinesin-like protein) (GG10_2)	1345	0
			AAC83230.1	rabkinesin6	1345	0
			AAD37806.1	AF153329_1 RAB6KIFL	1345	0
			AAH12999.1	AAH12999 Similar to RAB6 interacting, kinesin-like (rabkinesin 6)	1345	0
			NP_057279.1	M-phase phosphoprotein 1; mitotic kinesin-like protein	333	9e-91
			T17272	hypothetical protein DKFZp434B0435.1	333	9e-91
			CAB55962.1	hypothetical protein	333	9e-91
			BAB69456.1	mitotic kinesin-related protein	326	1e-88
			NP_004847.2	kinesin-like 5 isoform 2; mitotic kinesin-like 1	201	4e-51
			Q02241	KNS5_HUMAN Mitotic kinesin-like protein-1 (Kinesin-like protein 5)	201	4e-51
			CAA47628.2	mitotic kinase-like protein-1	201	4e-51
			NP_612565.1	kinesin-like 5 isoform 1; mitotic kinesin-like 1	201	4e-51
			AAH17705.1	AAH17705 kinesin-like 5 (mitotic kinesin-like protein 1)	201	4e-51



			AAA35805.1	episialin variant A precursor	298	2e-80
			AAA35807.1	episialin variant B precursor	298	2e-80
			AAD10858.1	MUC-1/Z mucin short variant	274	5e-73
			S48146	mucin 1 precursor, non-repetitive splice form Y [validated]	272	1e-72
			CAA56734.1	MUC1	272	1e-72
			AAD10857.1	MUC-1/Y mucin short variant	272	1e-72
			AAD27842.1	AF125525_1 MUC1/Y mucin precursor	271	3e-72
			AAD10856.1	MUC-1/X mucin short variant	214	4e-56
NM_008652		U:(C-IR) 3.11				
NP_032678.1	Mm.4594	U:(C-D) 2				
			NP_002457.1	v-myb myeloblastosis viral oncogene homolog (avian)-like 2; B-MYB; v-myb avian myeloblastosis viral oncogene homolog-like 2	1123	0
			P10244	MYBB_HUMAN Myb-related protein B (B-Myb)	1123	0
			S01991	transforming protein B-myb	1123	0
			CAA31655.1	B-myb protein (AA 1-700)	1123	0
			CAC08392.1	dJ1028D15.3 (v-myb avian myeloblastosis viral oncogene homolog-like 2)	1123	0
			AAH07585.1	v-myb avian myeloblastosis viral oncogene homolog-like 2	1123	0
			P10243	MYBA_HUMAN Myb-related protein A (A-Myb)	280	1e-74
			S03423	transforming protein A-myb	280	1e-74
			CAA31656.1	A-myb N-terminal region )2341 is 2nd base in codon)	280	1e-74
			AAB49038.1	alternatively spliced product using exon 9A	276	1e-73
			CAA36371.1	MYB protein (AA 1-637)	276	1e-73
				v-myb myeloblastosis viral oncogene homolog (avian); v-myb avian myeloblastosis viral oncogene homolog; Avian myeloblastosis viral (v-myb) oncogene homolog; c-myb	276	1e-73
			NP_005366.1			
			AAA52032.1	c-myb	276	1e-73
			XP_004256.3	similar to Myb proto-oncogene protein (C-myb)	276	1e-73
			P10242	MYB_HUMAN Myb proto-oncogene protein (C-myb)	276	1e-73
			AAB49039.1	c-myb gene product	276	1e-73

				AAC96326.1	MYB proto-oncogene protein		276	1e-73
				TVHUMB	transforming protein myb, splice form containing exon 9A		276	1e-73
				AAB49035.1	alternatively spliced product using exon 9B		276	1e-73
				AAB49036.1	alternatively spliced product using exon 8A		276	1e-73
NM_008168		U:(C-IR) 2.99						
		U:(C-D) 2.57						
NP_032194.1	Mm.2879	U:(IR-D) 2.41		Q16478	GLK5_HUMAN Glutamate receptor, ionotropic kainate 5 precursor (Glutamate receptor KA-2) (KA2) (Excitatory amino acid receptor 2) (EAA2)	1757	0	0
				I57936	glutamate receptor subunit	1757	0	0
				AAB22591.1	glutamate receptor subunit; EAA2; excitatory amino acid receptor 2	1757	0	0
				NP_002079.2	glutamate receptor, ionotropic, kainate 5	1625	0	0
				CAC80547.1	kainate receptor subunit KA2a	1625	0	0
				NP_055434.1	glutamate receptor, ionotropic, kainate 4; excitatory amino acid receptor 1	1254	0	0
				Q16099	GLK4_HUMAN Glutamate receptor, ionotropic kainate 4 precursor (Glutamate receptor KA-1) (KA1) (Excitatory amino acid receptor 1)(EAA1)	1254	0	0
				JH0826	glutamate ionotropic receptor EAA1 chain precursor	1254	0	0
				AAB29311.1	excitatory amino acid receptor 1; kainate receptor subunit EAA1	1254	0	0
				A54260	glutamate receptor 6 kainate-preferring precursor	704	0	0
				AAB31362.1	GluR6 kainate receptor=ionotropic-type glutamate receptor	704	0	0
				NP_068775.1	glutamate receptor, ionotropic, kainate 2	704	0	0
				Q13002	GLK2_HUMAN Glutamate receptor, ionotropic kainate 2 precursor (Glutamate receptor 6) (GluR-6) (GluR6) (Excitatory amino acid receptor 4) (EAA4)	704	0	0
				AAC50420.1	EAA4	704	0	0
				CAC67487.1	GluR6 kainate receptor	689	0	0
				CAC81020.1	kainate receptor subunit	687	0	0
				Q13003	GLK3_HUMAN Glutamate receptor, ionotropic kainate 3 precursor (Glutamate receptor 7) (GluR-7) (GluR7) (Excitatory amino acid receptor 5) (EAA5)	687	0	0
				NP_000822.1	glutamate receptor, ionotropic, kainate 3	687	0	0

				AAB60407.1	EAA5			687	0
				AAA95961.1	EAA3			685	0
NM_007765		U:(C-IR) 2.93							
NP_031791.1	Mm.22695	U:(C-D) 2.6		NP_001304.1		collapsin response mediator protein 1 (dihydropyrimidinase-like 1)		1036	0
				Q14194		DPY1_HUMAN Dihydropyrimidinase related protein-1 (DRP-1) (Collapsin response mediator protein 1) (CRMP-1)		1036	0
				JC5316		dihydropyrimidinase related protein 1		1036	0
				BAA11190.1		dihydropyrimidinase related protein-1		1036	0
				AAH00252.1		collapsin response mediator protein 1		1036	0
				AAH07613.1		collapsin response mediator protein 1		1036	0
				AAK55500.1		collapsin response mediator protein 1		963	0
				AAA93201.1		hCRMP-1		919	0
				NP_001377.1		dihydropyrimidinase-like 2; collapsin response mediator protein hCRMP-2		847	0
				Q16555		DPY2_HUMAN Dihydropyrimidinase related protein-2 (DRP-2) (Collapsin response mediator protein 2) (CRMP-2) (N2A3)		847	0
				JC5317		dihydropyrimidinase-related protein 2		847	0
				AAA93202.1		hCRMP-2		847	0
				BAA11191.1		dihydropyrimidinase related protein-2		847	0
				AAC05793.1		N2A3		847	0
				BAA86991.1		dihydropyrimidinase related protein 2		847	0
				NP_001378.1		dihydropyrimidinase-like 3		813	0
				Q14195		DPY3_HUMAN Dihydropyrimidinase related protein-3 (DRP-3) (Unc-33-like phosphoprotein) (ULIP protein) (Collapsin response mediator protein 4) (CRMP-4)		813	0
				JC5318		dihydropyrimidinase related protein 3		813	0
				BAA11192.1		dihydropyrimidinase related protein-3		813	0
				AAH39006.1		dihydropyrimidinase-like 3		813	0
				CAA69153.1		ULIP		810	0



				NP_006417.1	dihydropyrimidinase-like 4		781	0
				O14531	DPY4_HUMAN Dihydropyrimidinase related protein-4 (DRP-4) (ULP4 protein)		781	0
				BAA21886.1	dihydropyrimidinase related protein 4		781	0
				CAA71872.1	cytosolic phosphoprotein		749	0
				AAH07898.1	Similar to collapsin response mediator protein 1		712	0
NM_009872		U:(C-IR) 2.86						
NP_034002.1	Mm.15383 3	U:(C-D) 2.61		NP_003927.1	cyclin-dependent kinase 5, regulatory subunit 2; cyclin-dependent kinase 5 activator isoform p39i; NEURONAL CDK5 activator isoform		483	e-136
				Q13319	CD55_HUMAN Cyclin-dependent kinase 5 activator 2 precursor (CDK5 activator 2) (Cyclin-dependent kinase 5 regulatory subunit 2) (P39)(P39I)		483	e-136
				I39172	cyclin-dependent kinase 5 activator isoform p39i		483	e-136
				AAC50278.1	cyclin-dependent kinase 5 activator isoform p39i		483	e-136
				2202258A	cyclin-dependent kinase 5		483	e-136
				NP_003876.1	cyclin-dependent kinase 5, regulatory subunit 1; regulatory partner for cdk5 kinase; TPKII regulatory subunit		228	1e-59
					CD5R_HUMAN Cyclin-dependent kinase 5 activator 1 precursor (CDK5 activator 1) (Cyclin-dependent kinase 5 regulatory subunit 1) (Tau protein kinase II 23 kDa subunit) (TPKII regulatory subunit) (P23) (P25) (P35)		228	1e-59
				S50861	cyclin-dependent kinase 5 regulatory chain p35		228	1e-59
				CAA56587.1	regulatory partner for cdk5 kinase		228	1e-59
				AAH20580.1	AAH20580 cyclin-dependent kinase 5, regulatory subunit 1 (p35)		228	1e-59
				2019431A	cyclin-dependent kinase 5:SUBUNIT=p35		228	1e-59
				AAH26347.1	cyclin-dependent kinase 5, regulatory subunit 1 (p35)		226	4e-59
				AAH30792.1	cyclin-dependent kinase 5, regulatory subunit 1 (p35)		226	4e-59
				1H4L	D Chain D, Structure And Regulation Of The Cdk5-P25(Nck5a) Complex		217	2e-56
				1H4L	E Chain E, Structure And Regulation Of The Cdk5-P25(Nck5a) Complex		217	2e-56

NM_019964	Mm.2039	U:(C-IR) 2.84	XP_093388.1	similar to DnaJ homolog subfamily B member 8 (mDf6)	336	4e-92
NP_064348.1	2	U:(C-D) 3.13				
			NP_699161.1	hypothetical protein MGC33884	336	4e-92
			AAH29521.1	Similar to DnaJ (Hsp40) homolog, subfamily B, member 8	336	4e-92
			NP_005485.1	DnaJ (Hsp40) homolog, subfamily B, member 6 isoform b; Heat shock protein J2	258	7e-69
			BAA32209.1	MRJ	258	7e-69
			AAD43194.1	AF075601_1 heat shock J2 protein	258	7e-69
			AAF21257.1	AF060703_1 DnaJ homolog	258	7e-69
			BAA88770.1	DnaJ homolog	258	7e-69
			CAB66642.1	hypothetical protein	258	7e-69
			AAH00177.1	AAH00177 Similar to DnaJ (Hsp40) homolog, subfamily B, member 6	258	7e-69
			XP_052862.4	similar to DnaJ homolog	256	3e-68
			NP_490647.1	DnaJ (Hsp40) homolog, subfamily B, member 6 isoform a; Heat shock protein J2	249	6e-66
			O75190	DJB6_HUMAN DnaJ homolog subfamily B member 6 (Heat shock protein J2) (HSJ-2) (MSJ-1) (HHDJ1) (MRJ)	249	6e-66
			BAA88769.1	DnaJ homolog	249	6e-66
			AAH02446.1	AAH02446 MRJ gene for a member of the DnaJ protein family	249	6e-66
NM_008417		U:(C-IR) 2.82				
NP_032443.1	Mm.56930	U:(C-D) 2.47	NP_004965.1	potassium voltage-gated channel, shaker-related subfamily, member 2; voltage-gated potassium channel protein Kv1.2; potassium channel	880	0
			P16389	CIK2_HUMAN Potassium voltage-gated channel subfamily A member 2 (Potassium channel Kv1.2) (RBK2) (HBK5) (NGK1) (MK2) (HUKIV)	880	0
			I77466	potassium channel	880	0
			AAA36141.1	potassium channel	880	0
			NP_000208.1	potassium voltage-gated channel, shaker-related subfamily, member 1	662	0
			Q09470	CIK1_HUMAN Potassium voltage-gated channel subfamily A member 1 (Potassium channel Kv1.1) (HUK1) (HBK1)	662	0

				IS7680	potassium channel KCNA1	662	0
				AAA36139.1	potassium channel	662	0
				NP_002223.2	potassium voltage-gated channel, shaker-related subfamily, member 3; potassium channel protein; voltage-gated potassium channel; voltage-gated potassium channel protein Kv1.3; type n potassium channel	600	e-171
				P22001	CIK3_HUMAN Potassium voltage-gated channel subfamily A member 3 (Potassium channel Kv1.3) (HPCN3) (HGK5) (HUKII) (HLK3)	600	e-171
				AAB88073.1	voltage-gated potassium channel	600	e-171
				AAH35059.1	potassium voltage-gated channel, shaker-related subfamily, member 3	600	e-171
				A38101	potassium channel KCNA3	599	e-171
				AAA59457.1	potassium channel protein	599	e-171
				AAC31761.1	potassium channel	598	e-171
				AAA36425.1	potassium channel protein	595	e-170
				NP_002224.1	potassium voltage-gated channel, shaker-related subfamily, member 4; potassium voltage-gated channel, shaker-related subfamily, member 4-like; potassium channel KCNA4; shaker-related potassium channel Kv1.4; voltage-gated potassium channel; potassium channel protein; type A potassium channel; rapidly inactivating potassium channel; fetal skeletal muscle potassium channel; cardiac potassium channel; potassium channel 2; voltage-gated potassium channel protein Kv1.4	543	e-154
				A39922	potassium channel KCNA4	543	e-154
				AAA36140.1	potassium channel	543	e-154
				AAA61275.1	voltage-gated potassium channel	543	e-154
				P22459	CIK4_HUMAN Potassium voltage-gated channel subfamily A member 4 (Potassium channel Kv1.4) (HK1) (HPCN2) (HBK4) (HUKII)	541	e-153
				AAA60034.1	potassium channel protein	541	e-153
				NP_002226.1	potassium voltage-gated channel, shaker-related subfamily, member 6; voltage-gated potassium channel protein Kv1.6; human brain potassium channel-2	519	e-147
				P17658	CIK6_HUMAN Potassium voltage-gated channel subfamily A member 6 (Potassium channel Kv1.6) (HBK2)	519	e-147
				CAA35623.1	put. HBK2 protein (AA 1-529)	519	e-147
				S12787	potassium channel KCNA2	517	e-146

NM_013809 NP_038837.1	Mm.1023 12	U:(C-IR) 2.79 U:(C-D) 2.22	NP_000757.2	cytochrome P450, subfamily IIA (phenobarbital-inducible), polypeptide 13	563	e-160
			AAG35775.1	cytochrome P450 2A13	563	e-160
			Q16696	CPAD_HUMAN Cytochrome P450 2A13 (CYP1A13)	558	e-158
			AAB40519.1	cytochrome P450	558	e-158
			O4HUA6	coumarin 7-hydroxylase (EC 1.14.14.-) cytochrome P450 2A6	555	e-158
			AAA52067.1	cytochrome P450IIA3	555	e-158
			NP_000753.2	cytochrome P450, subfamily IIA (phenobarbital-inducible), polypeptide 6; coumarin 7-hydroxylase; cytochrome P450, subfamily IIA (phenobarbital-inducible), polypeptide 3; xenobiotic monooxygenase; flavoprotein-linked monooxygenase	553	e-157
			P11509	CPA6_HUMAN Cytochrome P450 2A6 (CYP1A6) (Coumarin 7-hydroxylase) (IIA3) (CYP2A3) (P450(I))	552	e-157
			CAA32118.1	P-450 IIA4 protein (AA 1-494)	552	e-157
			AAF13600.1	AF182275_1 cytochrome P450-2A6	551	e-157
			1609083A	cytochrome P450IIA	551	e-156
			CAA32097.1	cytochrome P-450IIA (AA 1 - 489)	551	e-156
			P20853	CPA7_HUMAN Cytochrome P450 2A7 (CYP1A7) (P450-IIA4)	543	e-154
			AAA52138.1	cytochrome P450IIA4	543	e-154
			C34271	cytochrome P450 2A4	543	e-154
NM_017402 NP_059098.1		U:(C-IR) 2.74 U:(C-D) 2.8	NP_003890.1	Rho guanine nucleotide exchange factor 7 isoform a; SH3 domain-containing proline-rich protein; PAK-interacting exchange factor beta	1135	0
			Q14155	PIXB_HUMAN Rho guanine nucleotide exchange factor 7 (PAK-interacting exchange factor beta) (Beta-Pix) (COOL-1) (p85)	1135	0
			BAA09763.1	The KIAA0142 gene is related to human KIAA0006 gene.	1135	0
			CAD38906.1	hypothetical protein	1014	0
			NP_663788.1	Rho guanine nucleotide exchange factor 7 isoform b; SH3 domain-containing proline-rich protein; PAK-interacting exchange factor beta	1014	0

				BAA04985.1	this sequence overlaps D13631, it covers 954..4359 of this sequence.	751	0
				XP_042963.2	similar to Rho guanine nucleotide exchange factor 6 (PAK-interacting exchange factor alpha) (Alpha-Pix) (COOL-2)	751	0
				NP_004831.1	Rac/Cdc42 guanine nucleotide exchange factor 6; PAK-interacting exchange factor, alpha; Rac/Cdc42 guanine exchange factor (GEF) 6; rho guanine nucleotide exchange factor 6	751	0
				Q15052	ARH6_HUMAN Rho guanine nucleotide exchange factor 6 (PAK-interacting exchange factor alpha) (Alpha-Pix) (COOL-2)	751	0
				AAH39856.1	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	751	0
				BAA02796.1	KIAA0006	504	e-142
				1BY1	A Chain A, Db1 Homology Domain From Beta-Pix	385	e-106
				AAH33768.1	Similar to Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	301	4e-81
NM_009819		U:(C-IR) 2.7					
NP_033949.1	Mm.34637	U:(C-D) 2.71		NP_004380.1	catenin (cadherin-associated protein), alpha 2; Catenin, alpha-2(cadherin-associated protein, related)	1684	0
				P26232	CTN2_HUMAN Alpha-2 catenin (Alpha-catenin related protein) (Alpha N-catenin)	1684	0
				AAA58407.2	cadherin-associated protein-related	1684	0
				A45011	alpha-catenin 2	1317	0
				XP_038221.1	similar to Alpha-1 catenin (Cadherin-associated protein) (AlphaE-catenin)	1317	0
				P35221	CTN1_HUMAN Alpha-1 catenin (Cadherin-associated protein) (Alpha E-catenin)	1317	0
				N0607	alpha-catenin 1	1317	0
				BAA02979.1	alpha-catenin	1317	0
				AAC99459.1	alphaE-catenin	1317	0
				AAH00385.1	Unknown (protein for MGC:8429)	1317	0
				BAA03530.1	'human alpha-catenin'	1313	0
				2023176A	alpha catenin	1313	0
				JC2542	alpha-2(E)-catenin	1290	0
				AAA18949.1	alpha2(E)-catenin	1290	0

			NP_001894.1	catenin (cadherin-associated protein), alpha 1, 102kDa; catenin (cadherin-associated protein), alpha 1 (102kD); catenin (cadherin-associated protein), alpha 1 (102kDa)	1286	0
			AAA86430.1	alpha1(E)-catenin	1286	0
			NP_037398.1	alpha-catenin-like protein	974	0
			AAF21801.1	AF091606_1 alphaT-catenin	974	0
			AAH31262.1	Similar to catenin (cadherin-associated protein), alpha 2	841	0
			1H6G	A Chain A, Alpha-Catenin M-Domain	389	e-107
			1H6G	B Chain B, Alpha-Catenin M-Domain	389	e-107
			XP_068797.2	similar to alpha(E)-catenin	380	e-105
NM_010437 NP_034567.1	Mm.4215 7	U:(C-IR) 2.68	NP_006725.2	human immunodeficiency virus type I enhancer binding protein 2; human immunodeficiency virus type I enhancer-binding protein 2	3799	0
			WMHUE2	HIV-EP2 enhancer-binding protein	3799	0
			CAA446596.1	MBP-2 (MHC Binding Protein-2)	3799	0
			AAF81365.1	human immunodeficiency virus type I enhancer-binding protein 2	3797	0
			P31629	ZEP2_HUMAN HUMAN IMMUNODEFICIENCY VIRUS TYPE I ENHANCER-BINDING PROTEIN 2 (HIV-EP2)	2698	0
			AAB88218.1	HIV-EP2/Schnurri-2	2698	0
			NP_078779.1	human immunodeficiency virus type I enhancer-binding protein 3	786	0
			AAK01082.1	AF278765_1 kappa B and V(D)J recombination signal sequences binding protein	786	0
			BAB13381.1	KIAA1555 protein	486	e-136
			NP_002105.1	human immunodeficiency virus type I enhancer binding protein 1; human immunodeficiency virus type I enhancer-binding protein 1	257	2e-67
			P15822	ZEP1_HUMAN Zinc finger protein 40 (Human immunodeficiency virus type I enhancer-binding protein 1) (HIV-EP1) (Major histocompatibility complex binding protein 1) (MBP-1) (Positive regulatory domain II binding factor 1) (PRDII-BF1)	257	2e-67
			A34203	DNA-binding protein PRDII-BF1	257	2e-67
			CAA35798.1	PRDII-BF1 protein (AA 1-2717)	257	2e-67
			AAA17534.1	DNA-binding protein	250	2e-65



			AAA16173.1	Wilson disease-associated protein		608	e-173
NM_008356		U:(C-IR) 2.61					
NP_032382.1	Mm.20855	U:(C-D) 2.38	NP_000631.1	interleukin 13 receptor, alpha 2 precursor; interleukin 13 binding protein; interleukin 13 receptor alpha 2 chain; IL-13 receptor	431	e-120	
			Q14627	I132_HUMAN Interleukin-13 receptor alpha-2 chain precursor (Interleukin-13 binding protein)	431	e-120	
			CAA64617.1	interleukin 13 receptor	431	e-120	
			AAB17170.1	interleukin-13 receptor	431	e-120	
			CAA70021.1	IL-13 receptor	431	e-120	
			CAD18962.1	dA204F4.1 (interleukin 13 receptor, alpha 2)	431	e-120	
			AAH20739.1	interleukin 13 receptor, alpha 2	431	e-120	
			AAH33705.1	interleukin 13 receptor, alpha 2	431	e-120	
			AAAG17965.1	AF089087_1 G protein-coupled receptor	411	e-114	
NM_022320	Mm.1527	U:(C-IR) 2.59					
NP_071715.1	80	U:(C-D) 3.35					
		U:(IR-D) 2.3					
			NP_005292.1	G protein-coupled receptor 35	409	e-113	
			Q9HC97	GP35_HUMAN Probable G protein-coupled receptor GPR35	409	e-113	
			AAC52028.1	G protein-coupled receptor	409	e-113	
NM_010174	Mm.2222	U:(C-IR) 2.54	CAA71305.1	mammary-derived growth inhibitor	241	5e-64	
NP_034304.1	0						
			NP_004093.1	fatty acid binding protein 3	240	1e-63	
			XP_049316.1	similar to Fatty acid-binding protein, heart (H-FABP) (Muscle fatty acid-binding protein) (M-FABP) (Mammary-derived growth inhibitor) (MDGI)	240	1e-63	
			P05413	FABH_HUMAN Fatty acid-binding protein, heart (H-FABP) (Muscle fatty acid-binding protein) (M-FABP) (Mammary-derived growth inhibitor) (MDGI)	240	1e-63	
			FZHUC	fatty acid-binding protein, cardiac and skeletal muscle - human	240	1e-63	



			CAA39889.1	muscle fatty-acid-binding protein (FABP)	240	1e-63
			AAB02555.1	fatty acid binding protein FABP	240	1e-63
			AAC99800.1	fatty acid binding protein	240	1e-63
			AAH07021.1	AAH07021 fatty acid binding protein 3, muscle and heart (mammary-derived growth inhibitor)	240	1e-63
			1G5W	A Chain A, Solution Structure Of Human Heart-Type Fatty Acid Binding Protein	238	6e-63
			1HMR	Fatty Acid Binding Protein (Human Muscle, M-Fabp) Complexed With One Molecule Of Elaidic Acid	238	6e-63
			1HMS	Fatty Acid Binding Protein (Human Muscle, M-Fabp) Complexed With One Molecule Of Elaidic Acid	238	6e-63
			1HMT	Fatty Acid Binding Protein (Human Muscle, M-Fabp) Complexed With One Molecule Of Elaidic Acid	238	6e-63
			2HMB	Fatty Acid Binding Protein (Holo Form, Human Muscle) (M-Fabp)	238	6e-63
			1714345A	fatty acid-binding protein	237	1e-62
			AAB29294.1	heart fatty acid binding protein; hFABP	214	9e-56
NM_007634		U:(C-IR) 2.52				
NP_031660.1	Mm.4008	U:(C-D) 2.12	AAB60342.1	cyclin F	1206	0
			P41002	CG2F_HUMAN G2/mitotic-specific cyclin F	1205	0
			AAH12349.1	cyclin F	1205	0
			NP_001752.1	cyclin F; G2/mitotic-specific cyclin F; F-box only protein 1	1197	0
			A55501	cyclin F	1197	0
			CAA85308.1	cyclin F [Homo sapiens]	1197	0
			NP_002338.1	lymphocyte antigen 6 complex, locus H	209	2e-54
NM_011837	Mm.2215	U:(C-IR) 2.5				
NP_035967.1	4	U:(C-D) 2.69				
		U:(IR-D) 2.06				
			O94772	LY6H_HUMAN Lymphocyte antigen Ly-6H precursor	209	2e-54

			BAA34115.1	Ly-6 gene family~another possible initiation codon is at nt position (162..164)	209	2e-54
			AAH28894.1	lymphocyte antigen 6 complex, locus H	209	2e-54
			AAH30192.1	lymphocyte antigen 6 complex, locus H	209	2e-54
NM_021050		U:(C-IR) 2.5	P13569	CFTR_HUMAN Cystic fibrosis transmembrane conductance regulator (CFTR) (cAMP-dependent chloride channel)	2207	0
NP_066388.1	Mm. 1562 1	U:(C-D) 2.36				
			DVHUCF	cystic fibrosis transmembrane conductance regulator	2207	0
			AAC13657.1	cystic fibrosis transmembrane conductance regulator	2207	0
			NP_000483.2	cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7); cystic fibrosis transmembrane conductance regulator; ATP-binding cassette, sub-family C member 7; CFTR/MRP	2202	0
			AAA35680.1	cystic fibrosis transmembrane conductance regulator	2202	0
			AAB46352.1	transmembrane chloride conductor protein	1523	0
			AAB46340.1	cystic fibrosis transmembrane conductance regulator	687	0
			AAH46341.1	coded for by human cDNA M96936 (NID:g180293)	630	e-180
			AAH41560.1	Similar to ATP-binding cassette, sub-family C (CFTR/MRP), member 4	402	e-111
			AAN17334.1	ATP-binding cassette protein C4 splice variant A	402	e-111
			AAH88745.1	multidrug resistance-associated protein	402	e-111
			NP_005836.1	ATP-binding cassette, sub-family C, member 4; canalicular multispecific organic anion transporter (ABC superfamily)	402	e-111
			O15439	MRP4_HUMAN Multidrug resistance-associated protein 4 (MRP/cMOAT-related ABC transporter) (Multi-specific organic anion transporter-B) (MOAT-B)	402	e-111
			AAC27076.1	ABC transporter MOAT-B	402	e-111
			AAC27077.1	ABC transporter MOAT-B isoform	353	2e-96
AF363457		U:(C-IR) 2.5				
AAK60137.1	Mm.13083 2	U:(C-D) 2.33	NP_077015.1	caspase recruitment domain protein 14 isoform 1; CARD-containing	1257	0
			Q9BXL6	CARE_HUMAN Caspase recruitment domain protein 14 (CARD-containing MAGUK protein	1257	0

			AAAG53403.1	AF322642_1 caspase recruitment domain protein 14	1257	0
			AAK54453.1	CARD-containing MAGUK 2 protein	1257	0
			AAH18142.1	Similar to caspase recruitment domain protein 14	953	0
			NP_438170.1	caspase recruitment domain protein 14 isoform 2; CARD-containing	407	e-113
			AAH01326.1	Unknown (protein for MGC:5551)	407	e-113
			Q9BXL7	CARB_HUMAN Caspase recruitment domain protein 11 (CARD-containing MAGUK protein)	202	3e-51
			AAAG53402.1	AF322641_1 caspase recruitment domain protein 11	202	3e-51
			NP_115791.2	caspase recruitment domain family, member 11; card-maguk protein 1;	202	3e-51
			AAL344460.1	AF352576_1 CARD-containing MAGUK protein CARMA1	202	3e-51
			BAB84875.1	FLJ00120 protein	202	3e-51
NM_009203		U:(C-IR) 2.49				
NP_033229.1	Mm.12846	U:(C-D) 2.42	P_653186.2	urate anion exchanger 1 isoform a; organic anion transporter 4-like; urate transporter 1; solute carrier family 22 member 12	780	0
			AAK68156.1	AC044790_3 RST	780	0
			BAB96750.1	URAT1	780	0
			BAB68364.1	organic anion transporter 4 like protein	688	0
			NP_060954.1	solute carrier family 22 member 11; organic anion transporter 4	502	e-142
			BAA95316.1	organic anion transporter 4	502	e-142
			AAK68155.1	AC044790_2 OAT4	502	e-142
			AAH34384.1	solute carrier family 22 (organic anion/cation transporter), member 11	502	e-142
			NP_695008.1	solute carrier family 22 member 6 isoform b; renal organic anion transporter 1; para-aminohippurate transporter	457	e-128
			AAD19356.1	organic anion transporter 1	457	e-128
			BAA75073.1	hOAT1-2	457	e-128
			AAD55356.1	AF124373_1 organic anion transporter 1	457	e-128
			AAH33682.1	solute carrier family 22 (organic anion transporter), member 6	457	e-128
			AAC70004.1	putative renal organic anion transporter 1	457	e-128



			NP_001454.1	frizzled-related protein; Fritz; Frzb-1; fre; frizzled ( <i>Drosophila</i> ) homolog-related; fzrb; hfiz	593	e-169
			AAC50736.1	Frzb precursor	593	e-169
			AAB51298.1	Fritz	593	e-169
			NP_003005.1	secreted frizzled-related protein 4; secreted frizzled-related protein 4	312	2e-84
			AAC04617.1	fzrHE	312	2e-84
NM_053115	Mm.2870	U:(C-IR)	NP_003491.1	acyl-Coenzyme A oxidase 2, branched chain; Peroxisomal branched chain acyl-CoA oxidase	1033	0
NP_444345.1	0	2.42	Q99424	CAO2_HUMAN Acyl-coenzyme A oxidase 2, peroxisomal (Branched-chain acyl-CoA oxidase) (BRCA-Cox) (Trihydroxycoprostanoyl-CoA oxidase) (THCCox) (THCA-CoA oxidase)	1033	0
			CAA64489.1	branched chain acyl-CoA oxidase	1033	0
			CAB65596.1	peroxisomal branched chain acyl-CoA oxidase	1033	0
			AAB30019.2	peroxisomal acyl-coenzyme A oxidase	536	e-152
			Q15067	CAO1_HUMAN Acyl-coenzyme A oxidase 1, peroxisomal (Palmitoyl-CoA oxidase) (AOX)	535	e-152
			I38095	acyl-CoA oxidase (EC 1.3.3.6), peroxisomal	534	e-151
			CAA50574.1	peroxisomal acyl-CoA oxidase	534	e-151
			AAH08767.1	AAH08767 Similar to acyl-Coenzyme A oxidase 1, palmitoyl	532	e-151
			AAH10425.1	AAH10425 Unknown (protein for MGC:15225)	531	e-150
			AAA18595.1	peroxisomal fatty acyl-coA oxidase	530	e-150
			NP_009223.1	acyl-Coenzyme A oxidase isoform b; acyl-coenzyme A oxidase 1	526	e-149
			A54942	acyl-CoA oxidase (EC 1.3.3.6), peroxisomal splice form I	526	e-149
			AAA19113.1	acyl-CoA oxidase	526	e-149
			NP_004026.1	acyl-Coenzyme A oxidase isoform a; acyl-coenzyme A oxidase 1	523	e-148
			B54942	acyl-CoA oxidase (EC 1.3.3.6), peroxisomal splice form II	523	e-148
			AAA19114.1	acyl-CoA oxidase	523	e-148
			NP_003492.1	acyl-Coenzyme A oxidase 3, pristanoyl	268	2e-71
			O15254	CAO3_HUMAN Acyl-coenzyme A oxidase 3, peroxisomal (Pristanoyl-CoA oxidase)	268	2e-71

			CAA72214.1	pristanoyl-CoA oxidase		268	2e-71
		U:(C-IR) 2.42	NP_001731.1	calbindin 2 full length protein isoform; calbindin 2, (29kD, calretinin); calbindin D29K		371	e-102
			P22676	CLB2_HUMAN Calretinin (CR) (29 kDa calbindin)		371	e-102
			A60253	calretinin		371	e-102
			CAA39991.1	calretinin		371	e-102
			1709139B	calretinin		371	e-102
			AAH15484.1	AAH15484 calbindin 2, (29kD, calretinin)		371	e-102
			NP_004920.1	calbindin 1; calbindin 1, (28kD)		249	5e-66
			P05937	CABV_HUMAN Calbindin (Vitamin D-dependent calcium-binding protein, avian-type) (Calbindin D28) (D-28K)		249	5e-66
			S00234	calcium-binding protein, vitamin D-dependent		249	5e-66
			CAA29860.1	calbindin (AA 1-261)		249	5e-66
			AAC62230.1	27kDa calbindin		249	5e-66
			AAD08724.1	calbindin 1		249	5e-66
			AAH06478.1	AAH06478 calbindin 1, (28kD)		249	5e-66
			AAH20864.1	AAH20864 calbindin 1, (28kD)		249	5e-66
			1403296A	calbindin 27kD		249	5e-66
			1709139A	calbindin D28K		249	5e-66
			NP_009019.1	calbindin 2 isoform 22k; calbindin 2, (29kD, calretinin); calbindin D29K		199	1e-50
			NP_009018.1	calbindin 2 isoform 20k; calbindin 2, (29kD, calretinin); calbindin D29K		198	1e-50
NM_013612 NP_038640.1		U:(C-IR) 2.38	XP_002585.4	similar to Natural resistance-associated macrophage protein 1 (NRAMP 1)		905	0
			P49279	NRM1_HUMAN Natural resistance-associated macrophage protein 1 (NRAMP 1)		905	0
			I55679	integral membrane protein		905	0
			AAAS7521.1	integral membrane protein		905	0
			BAA08908.1	Nramp		905	0
			AAAG15405.1	natural resistance-associated macrophage protein 1		905	0

			BAA08907.1	Nramp		904	0
			JC4095	natural resistance-associated macrophage protein NRAMP 1		889	0
			NP_000569.1	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 1; natural resistance-associated macrophage protein 1 (might include Leishmaniasis); solute carrier family 11 (sodium/phosphate symporters), member 1		887	0
			CAA57541.1	NRAMP		887	0
			BAA07370.1	Nramp		818	0
			CAD38517.1	divalent metal transporter		649	0
			NP_000608.1	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2; natural resistance-associated macrophage protein 2		649	0
			BAA24933.1	NRAMP2		649	0
			AAC21460.1	natural resistance-associated macrophage protein 2		649	0
			AAC18078.1	NRAMP2 iron transporter		649	0
			AAH02592.1	AAH02592 solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2		649	0
			P49281	NRM2_HUMAN Natural resistance-associated macrophage protein 2 (NRAMP 2) (Divalent metal transporter 1) (DMT1)		648	0
			AAC21459.1	natural resistance-associated macrophage protein 2 non-IRE form		648	0
			AAC21461.1	natural resistance-associated macrophage protein 2		648	0
			BAB93467.1	natural resistance-associated macrophage protein 2 non-IRE form		648	0
			BAA34374.1	natural resistance-associated macrophage protein 2		633	0
			I57022	integral membrane protein		629	e-180
			AAA79219.1	integral membrane protein		629	e-180
NM_020503 NP_065249.1	Mm.1038 03	U:(C-IR) 2.38	NP_062545.1	taste receptor T2R1; taste receptor, family B, member 7; taste receptor, type 2, member 1		260	2e-69
			AAF43902.1	AF227129_1 candidate taste receptor T2R1		260	2e-69
NM_026091 NP_080367.1	Mm.2771 1	U:(C-IR) 2.36	BAB14854.1	unnamed protein product		323	4e-88
			CAC17545.1	dJ1009E24.3 (novel protein)		323	4e-88

			AAH12196.1	AAH12196 Unknown (protein for MGC:4349)		323	4e-88
			AAH24036.1	chromosome 20 open reading frame 27		323	4e-88
			NP_060344.1	chromosome 20 open reading frame 27		321	1e-87
			BAA91252.1	unnamed protein product		321	1e-87
NM_008123							
NP_032149.1	Mm.56907	U:(C-IR) 2.35	P48165	CXA8_HUMAN Gap junction alpha-8 protein (Connexin 50) (Cx50) (Lens fiber protein MP70)		679	0
			AAF32309.1	AF217524_1 gap junction protein alpha 8		679	0
			NP_005258.1	gap junction protein, alpha 8, 50kDa (connexin 50); gap junction membrane channel protein alpha-8; connexin 50; Gap junction membrane channel protein alpha-8 (connexin 50); gap junction protein, alpha 8, 50kD (connexin 50)		673	0
			I39176	intrinsic membrane protein MP70		673	0
			AAA77062.1	gap junction membrane channel protein alpha-		673	0
			NP_068773.2	gap junction protein, alpha 3, 46kDa (connexin 46); gap junction protein, alpha 3, 46kD (connexin 46)		332	8e-91
			CAC16957.1	bA264J4.3 (novel connexin (gap junction protein))		332	8e-91
			Q9Y6H8	CXA3_HUMAN Gap junction alpha-3 protein (Connexin 46) (Cx46)		332	8e-91
			AAD42925.1	gap-junction protein alpha 3		332	8e-91
			NP_005257.2	gap junction protein, alpha 5, 40kDa (connexin 40); gap junction protein, alpha 5, 40kD (connexin 40)		308	2e-83
			P36382	CXA5_HUMAN Gap junction alpha-5 protein (Connexin 40) (Cx40)		308	2e-83
			AAA91833.1	connexin 40		308	2e-83
			AAD37801.1	AF151979_1 connexin 40		308	2e-83
			AAA60457.2	connexin40		308	2e-83
			AAH13313.1	AAH13313 gap junction protein, alpha 5, 40kD (connexin 40)8		308	2e-83
			I38429	connexin40		308	2e-83
			AAK55516.1	AF271261_1 connexin 58		280	4e-75
			NP_110399.1	connexin 59; gap junction alpha 10		280	4e-75



			P57773	CXAA_HUMAN Gap junction alpha-10 protein (Connexin 59) (Cx59)	280	4e-75
			AAAG09406.1	AF179597_1 connexin 59	280	4e-75
			NP_115991.1	connexin 62	279	8e-75
			AAK51676.1	AF296766_1 connexin 62	279	8e-75
			CAC93847.1	connexin62	279	8e-75
			AAD56533.1	AF180815_1 truncated connexin 37 polymorph	267	3e-71
NM_013473			XP_036593.2	similar to annexin A8	596	e-170
NP_038501.2	U:(C-IR) Mm.3267 2.35					
			AAH04376.1	AAH04376 annexin A8	596	e-170
			NP_001621.1	annexin VIII; Annexin VII	595	e-169
			P13928	ANX8_HUMAN Annexin A8 (Annexin VIII) (Vascular anticoagulant-beta) (VAC-beta)	595	e-169
			CAA34650.1	vascular anticoagulant-beta (AA 1 - 327)	595	e-169
			LUHU8	annexin VIII	593	e-169
			AAB46383.1	anexin VIII	590	e-168
			XP_054475.4	similar to annexin A8	575	e-165
			P09525	ANX4_HUMAN Annexin A4 (Annexin IV) (Lipocortin IV) (Endonexin I) (Chromobindin 4) (Protein II) (P32.5) (Placental anticoagulant protein II) (PAP-II) (PP4-X) (35-beta calcimedlin) (Carbohydrate-binding protein P33/P41) (P33/41)	337	4e-92
			NP_001144.1	annexin IV; annexin IV (placental anticoagulant protein II); placental anticoagulant protein II	337	4e-92
			XP_031596.2	similar to annexin IV; annexin IV (placental anticoagulant protein II); placental anticoagulant protein II	337	4e-92
			A42077	annexin IV	337	4e-92
			AAA51740.1	annexin IV (placental anticoagulant protein II)	337	4e-92
			BAA11227.1	annexin IV (carbohydrate-binding protein p33/41)	337	4e-92
			AAH00182.1	AAH00182 annexin A4	337	4e-92
			AAH11659.1	AAH11659 Similar to annexin A4	337	4e-92
			AAC41689.1	protein PP4-X	337	4e-92

	1ANW	A Chain A, Annexin V	328	2e-89
	1ANW	B Chain B, Annexin V	328	2e-89
	1ANX	A Chain A, Annexin V	328	2e-89
	1ANX	B Chain B, Annexin V	328	2e-89
	1ANX	C Chain C, Annexin V	328	2e-89
	NP_001145.1	annexin V; endonexin II; anchorin CII; lipocortin V; placental anticoagulant protein I	328	2e-89
	P08758	ANX5_HUMAN Annexin V (Lipocortin V) (Endonexin II) (Calphobindin I) (CBP-I) (Placental anticoagulant protein I) (PAP-I) (PP4) (Thromboplastin inhibitor) (Vascular anticoagulant-alpha) (VAC-alpha) (Anchorin CII)	328	2e-89
	AQHUP	annexin V [validated]	328	2e-89
	1AVH	A Chain A, Annexin V (Hexagonal Crystal Form)	328	2e-89
	1AVH	B Chain B, Annexin V (Hexagonal Crystal Form)	328	2e-89
	1HAK	A Chain A, Crystal Structure Of Recombinant Human Placental Annexin V Complexed With K-201 As A Calcium Channel Activity Inhibitor	328	2e-89
	1HAK	B Chain B, Crystal Structure Of Recombinant Human Placental Annexin V Complexed With K-201 As A Calcium Channel Activity Inhibitor	328	2e-89
	1AVR	Annexin V (Rhombohedral Crystal Form)	328	2e-89
	CAA30985.1	VAC protein (AA 1-320)	328	2e-89
	AAA35570.1	anticoagulant precursor (5' end put.); putative	328	2e-89
	AAA52386.1	endonexin II	328	2e-89
	AAB59545.1	anticoagulant protein 4	328	2e-89
	BAA00122.1	blood coagulation inhibitor	328	2e-89
	AAA36166.1	lipocortin-V	328	2e-89
	AAB40047.1	annexin V	328	2e-89
	AAB60648.1	annexin V	328	2e-89
	AAH01429.1	AAH01429 annexin A5	328	2e-89
	AAH04993.1	AAH04993 annexin A5	328	2e-89
	AAH12804.1	AAH12804 Similar to annexin A5	328	2e-89
	AAH12822.1	AAH12822 Similar to annexin A5	328	2e-89

			1512315A	calphobindin		328	2e-89
			1313303A	coagulation inhibitor		328	2e-89
NM_008075							
NP_032101.1	Mm.14116	U:(C-IR) 2.33	NP_002033.1	gamma-aminobutyric acid (GABA) receptor, rho 1; gamma-aminobutyric acid (GABA) A receptor, rho-1		881	0
			P24046	GAR1_HUMAN Gamma-aminobutyric-acid receptor rho-1 subunit precursor (GABA(A) receptor)		881	0
			A38627	gamma-aminobutyric acid receptor A rho-1 chain precursor		881	0
			AAA52509.1	gamma-aminobutyric acid receptor type A rho-1 subunit		881	0
			P28476	GAR2_HUMAN Gamma-aminobutyric-acid receptor rho-2 subunit precursor (GABA(A) receptor)		654	0
			CAC07339.1	dJ131H7.1 (gamma-aminobutyric acid (GABA) receptor rho 2)		654	0
			NP_002034.1	gamma-aminobutyric acid (GABA) receptor, rho 2 precursor		652	0
			A38079	gamma-aminobutyric acid receptor rho-2 chain precursor		652	0
			AAA52510.1	gamma-amino butyric acid		652	0
			XP_116036.2	similar to Gamma-aminobutyric-acid receptor rho-3 subunit precursor (GABA(A) receptor)		459	e-129
			NP_068712.1	gamma-aminobutyric acid (GABA) A receptor, beta 3, isoform 2 precursor		315	2e-85
			NP_000805.1	gamma-aminobutyric acid (GABA) A receptor, beta 3, isoform 1 precursor		315	2e-85
			P28472	GAB3_HUMAN Gamma-aminobutyric-acid receptor beta-3 subunit precursor (GABA(A) receptor)		315	2e-85
			A55275	gamma-aminobutyric acid A receptor beta 3 chain splice form 1		315	2e-85
			AAA52511.1	GABA-alpha receptor beta-3 subunit		315	2e-85
			AAH10641.1	gamma-aminobutyric acid (GABA) A receptor, beta 3		312	1e-84
			NP_000806.1	gamma-aminobutyric acid (GABA) A receptor, delta		305	2e-82
			O14764	GAD_HUMAN Gamma-aminobutyric-acid receptor delta subunit precursor (GABA(A) receptor)		305	2e-82
			AAB70007.1	GABA-A receptor delta subunit		305	2e-82
			AAH33801.1	gamma-aminobutyric acid (GABA) A receptor, delta		302	2e-81

			NP_000804.1	gamma-aminobutyric acid (GABA) A receptor, beta 2, isoform 2		302	2e-81
			P47870	GAB2 HUMAN Gamma-aminobutyric-acid receptor beta-2 subunit precursor (GABA(A) receptor)		302	2e-81
			AAB29370.1	gamma-aminobutyric acid A receptor beta 2 subunit; (GABA)A receptor beta 2 subunit		302	2e-81
			AAB33983.1	GABAA receptor beta 2 subunit		302	2e-81
NM_008009							
NP_032035.1	Mm.46053	U:(C-IR) 2.32	NP_005121.1	heparin-binding growth factor binding protein		268	2e-71
			A41178	heparin-binding growth factor-binding protein precursor		268	2e-71
			AAA58636.1	heparin binding protein		268	2e-71
			AAD39216.1	AF149412_1 HBP17 heparin-binding and FGF-binding protein		268	2e-71
			AAH03628.1	heparin-binding growth factor binding protein		268	2e-71
			AAH08910.1	heparin-binding growth factor binding protein		268	2e-71
NM_008352		U:(C-IR) 2.29		interleukin 12B precursor; natural killer cell stimulatory factor-2; interleukin 12B; cytotoxic lymphocyte maturation factor 2, p40; interleukin-12 beta chain; interleukin 12, p40; natural killer cell stimulatory factor, 40 kD subunit; IL23, subunit p40			
NP_032378.1		U:(C-D) 2.24	NP_002178.2	I12B_HUMAN Interleukin-12 beta chain precursor (IL-12B) (Cytotoxic lymphocyte maturation factor 40 kDa subunit) (CLMF p40) (NK cell stimulatory factor chain 2) (NKSF2)	431	e-120	
			P29460	interleukin 12B precursor	431	e-120	
			A38957	cytotoxic lymphocyte maturation factor 40 kDa subunit	431	e-120	
			AAA35695.1	AF180563_1 interleukin 12, P40	431	e-120	
			AAD56386.1	interleukin 12 p40 subunit	431	e-120	
			AAG32620.1	AF512686_1 interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic lymphocyte maturation factor 2, p40)	431	e-120	
			AAM34792.1	natural killer cell stimulatory factor	429	e-120	
			AAA59938.1	A Chain A, The P40 Domain Of Human Interleukin-12	400	e-111	
			1F42	A Chain A, Human Interleukin-12	400	e-111	
			1F45				

NM_019980		U:(C-IR) 2.28	BAB32547.1	small integral membrane protein of lysosome/late endosome	234	5e-61
NP_064364.1	Mm.2111 9	U:(C-D) 2.11				
			NP_004853.1	LPS-induced TNF-alpha factor	178	3e-56

			Q99732	LITF_HUMAN Lipopolysaccharide-induced tumor necrosis factor-alpha factor (LPS-induced TNF-alpha factor) (P53-induced protein 7)	178	3e-56
			AAB36550.1	LPS-Induced TNF-Alpha Factor	178	3e-56
			AAC39530.1	Pig7	178	3e-56
NM_011562		U:(C-IR) 2.28	AAH22393.1	teratocarcinoma-derived growth factor 1	239	1e-62
NP_035692.1	Mm.5090	U:(C-D) 2.03				
			NP_003203.1	teratocarcinoma-derived growth factor 1	238	2e-62
			P13385	CRI1_HUMAN Teratocarcinoma-derived growth factor 1 (Epidermal growth factor-like cripto protein CR1) (Cripto-1 growth factor) (CRGF)	238	2e-62
			A30362	teratocarcinoma-derived growth factor 1	238	2e-62
			CAA32467.1	cripto protein (AA 1-188)	238	2e-62
			AAA61134.1	teratocarcinoma-derived growth factor 1	238	2e-62
			P51864	CRI2_HUMAN Teratocarcinoma-derived growth factor 2 (Epidermal growth factor-like cripto protein CR3) (Cripto-3 growth factor)	235	2e-61
			AAA61135.1	teratocarcinoma-derived growth factor 3	235	2e-61
			AAB46353.1	EGF repeat containing protein; HUMTDGF1A Human (clone CR)	235	2e-61
				teratocarcinoma-derived growth factor 1 (TDGFI) gene P13385; coded for by human cDNAs M96956 (NID:g339432), X14253 (NID:g30220) and M96955 (NID:g339430)		
			AAG49538.1	AF251549_1 cripto 3	235	2e-61
			AAG49539.1	AF251550_1 cripto 3	235	2e-61
			A39787	teratocarcinoma-derived growth factor	235	2e-61
			XP_092153.1	similar to teratocarcinoma-derived growth factor 1	207	6e-53
			XP_083967.1	similar to acyl-malonyl condensing enzyme	186	5e-88
NM_019871		U:(C-IR) 2.27				
NP_063924.1	Mm.6211					
			NP_689675.1	hypothetical protein FLJ40154	186	5e-88



		AAH39263.1	Similar to glutamate receptor, ionotropic, delta 1	1202	0
		NP_001501.1	glutamate receptor, ionotropic, delta 2; GluR-delta-2	1141	0
		O43424	GRD2_HUMAN Glutamate receptor delta-2 subunit precursor	1141	0
		AAC39579.1	glutamate receptor delta-2 subunit	1141	0
		NP_000821.1	glutamate receptor, ionotropic, kainate 1; human glutamate receptor (GLUR5)	362	2e-99
		P39086	GLK1_HUMAN Glutamate receptor, ionotropic kainate 1 precursor (Glutamate receptor 5) (GluR-5) (GluR5) (Excitatory amino acid receptor 3) (EAA3)	362	2e-99
		I58178	glutamate receptor	362	2e-99
		AAA52568.1	glutamate receptor	362	2e-99
		CAC80546.1	glutamate receptor subunit GluR5	359	1e-98
		AAA95961.1	EAA3	357	8e-98
		CAC80548.1	glutamate/kainate receptor subtype GluR7	346	1e-94
		NP_000822.1	glutamate receptor, ionotropic, kainate 3	344	5e-94
		AAB60407.1	EAA5	344	5e-94
NM_011427		AAD17332.1	zinc finger protein	442	e-124
NP_035557.1	Mm.2093				
		NP_005976.2	snail 1 homolog; snail 1 zinc finger protein	442	e-124
		O95863	SNAIL_HUMAN Zinc finger protein SNAIL (Snail protein homolog) (Snail protein)	442	e-124
		CAB52414.1	SNAIL protein	442	e-124
		AAD52986.1	AF155233_1 snail zinc finger protein	442	e-124
		CAC07340.1	dJ710H13.1 (snail 1 (drosophila homolog), zinc finger protein)	442	e-124
		AAH12910.1	AAH12910 Unknown (protein for MGC:21748)	442	e-124
		XP_065615.1	similar to snail 1 (drosophila homolog), zinc finger protein	355	1e-97
		AAF32527.1	AF131208_1 snail protein	250	3e-66
		NP_003059.1	snail 2; neural crest transcription factor SLUG; slug (chicken homolog), zinc finger protein	249	6e-66
		O43623	SLUG_HUMAN Zinc finger protein SLUG (Neural crest transcription factor Slug) (Snail homolog 2)	249	6e-66
		AAC34288.1	zinc finger protein slug	249	6e-66



				AAD55240.1	AF084243_1 zinc finger protein SLUG	249	6e-66
				AAH14890.1	AAH14890 slug (chicken homolog), zinc finger protein	249	6e-66
				AAH15895.1	AAH15895 slug (chicken homolog), zinc finger protein	249	6e-66
NM_021546	Mm.1437	U:(C-IR)		AAL01118.1	AF409141_1 NIP1	477	e-134
NP_067521.1	48	2.26		NP_112508.1	amyloid beta (A4) precursor protein-binding, family A, member 2 binding protein, isoform 1; synaptotagmin interacting protein STIP3; X11L-binding protein 51; amyloid beta (A4) precursor protein-binding, family A, member 2; synaptotagmin interacting protein 2; neuronal calcium-binding protein NECAB3	475	e-134
				AAG28415.1	AF193759_1 neuronal calcium binding protein NECAB3	475	e-134
				CAD37360.1	dJ63M2.4.1 (amyloid beta (A4) precursor protein-binding family A, member 2 protein, variant 1)	397	e-110
				NP_112509.1	amyloid beta (A4) precursor protein-binding, family A, member 2 binding protein, isoform 2; synaptotagmin interacting protein STIP3; X11L-binding protein 51; amyloid beta (A4) precursor protein-binding, family A, member 2; synaptotagmin interacting protein 2; neuronal calcium-binding protein NECAB3	358	2e-98
				BAB16413.1	X11L-binding protein 51	358	2e-98
				NP_071746.1	synaptotagmin interacting protein 1	254	3e-67
				BAC04568.1	unnamed protein product	254	3e-67
				AAG28412.1	AF193756_1 neuronal calcium binding protein NECAB1	196	7e-50
NM_025746	Mm.4614	U:(C-IR)		2208307A	PNG gene	206	9e-53
NP_080022.1	2	2.24					
AK010751							
AAN60072.1	Mm.29522	U:(C-IR)		AAL23683.1	MARK4 serine/threonine protein kinase	183	9e-51
				BAC11510.1	unnamed protein product	183	9e-51
				AAM55491.1	MAP/microtubule affinity-regulating kinase-like 1	183	9e-51
				BAC03375.1	microtubule affinity-regulating kinase-like1	183	9e-51

			BAB55238.1	unnamed protein product		183	9e-51
		U:(C-IR) 2.22	BAB21531.1	beta-1,3-N-acetylglucosaminyltransferase bGnT-3		508	e-144
NM_028189 NP_082465.1	Mm.2885 6	U:(C-IR) 2.41	NP_055071.1	beta-1,3-N-acetylglucosaminyltransferase bGnT-3; type II membrane protein; transmembrane protein 3; core 1 extending beta-1,3-N-acetylglucosaminyltransferase; beta-1,3-galactosyltransferase; beta-1,3-galactase 8; beta3gal-T8; UDP-galactose:beta-N-acetylglucosamine beta-1,3-galactosyltransferase 8; beta-3-GX-T8		506	e-143
			Q9Y2A9	B3G8_HUMAN Beta-1,3-galactosyltransferase 8 (Beta-1,3-GalTase 8) (Beta3Gal-T8) (b3Gal-T8) (UDP-galactose:beta-N-acetylglucosamine beta-1,3-galactosyltransferase 8) (UDP-Gal:beta-GlcNAc beta-1,3-galactosyltransferase 8) (Beta-3-Gx-T8) (Core 1 extending beta-1,3-N-acetylglucosaminyltransferase) (Core1-beta3GlcNAcT)		506	e-143
			BAA76497.1	type II membrane protein		506	e-143
			AAK00849.1	AF293973_1 core 1 extending beta-1,3-N-acetylglucosaminyltransferase		506	e-143
			CAC45044.1	beta-1,3-galactosyltransferase		506	e-143
			CAC82374.1	beta 1,6-GlcNAc-transferase		458	e-128
			NP_619651.1	beta-1,3-N-acetylglucosaminyltransferase protein		332	1e-90
			BAB88882.1	beta-1,3-N-acetylglucosaminyltransferase 6		332	1e-90
			AAH25357.1	Unknown (protein for IMAGE:4907098)		298	3e-80
			NP_660279.1	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 7; hypothetical gene supported by AK000770		266	1e-70
			AAM61770.1	AF502430_1 beta 1,3-N-acetylglucosaminyltransferase 7		266	1e-70
			CAC45045.1	beta-1,3-galactosyltransferase		254	4e-67
			BAC04622.1	unnamed protein product		253	9e-67
			CAC82375.1	beta 1,3 galactosyltransferase		253	9e-67
			AAL37219.1	AF321825_1 beta-1,3-galactosyltransferase-related protein		253	9e-67
NM_008522 NP_032548.1	Mm.7612	U:(C-IR) 2.22	AAA59479.1	neutrophil lactoferrin		1038	0

				P02788	TRFL_HUMAN Lactotransferrin precursor (Lactoferrin) [Contains: Lactoferrin A; Lactoferrin B; Lactoferrin C]	1038	0
				TFHUL	lactotransferrin precursor	1038	0
				AAB60324.1	lactoferrin	1038	0
				AAH15822.1	lactotransferrin	1036	0
				AAH22347.1	lactotransferrin	1035	0
				CAA37116.1	precursor lactoferrin (709 AA)	1035	0
				AAA36159.1	lactoferrin	1035	0
				AAN11304.1	lactoferrin	1035	0
				AAA59511.1	lactoferrin	1035	0
				AAG48753.1	lactoferrin precursor	1034	0
				AAN63998.1	lactotransferrin precursor	1034	0
				AAH15823.1	lactotransferrin	1033	0
				NP_002334.1	lactotransferrin	1032	0
				CAA37914.1	precursor (AA -19 to 692)	1032	0
NM_009637							
NP_033767.1	Mm.86453	U:(C-IR)	2.22				
				XP_058567.1	similar to AE binding protein 2; AE-binding protein 2	562	e-160
				NP_694939.1	hypothetical protein MGC17922	562	e-160
				AAH15624.1	AAH15624 Similar to AE-binding protein 2	562	e-160
				AAH22220.1	Unknown (protein for MGC:17922)	562	e-160
NM_010198	Mm.5723	U:(C-IR)	2.22	NP_004103.1	fibroblast growth factor 11; fibroblast growth factor homologous factor 3	444	e-125
NP_034328.1	8			Q92914	FGFB_HUMAN Fibroblast growth factor-11 (FGF-11) (Fibroblast growth factor homologous factor 3) (FHF-3)	444	e-125
				AAB18915.1	fibroblast growth factor homologous factor 3	444	e-125
				AAL15439.1	fibroblast growth factor 11	444	e-125
				AAM11871.1	fibroblast growth factor 11	444	e-125
				AAH32502.1	fibroblast growth factor 11	444	e-125

			NP_004106.1	fibroblast growth factor 14; fibroblast growth factor homologous factor 4	273	1e-73
			Q92915	FGFE_HUMAN Fibroblast growth factor-14 (FGF-14) (Fibroblast growth factor homologous factor 4) (FHF-4)	273	1e-73
			AAB18916.1	fibroblast growth factor homologous factor 4	273	1e-73
			AAN16025.1	AE014303 1 FHF4	273	1e-73
			NP_066360.1	fibroblast growth factor 12 isoform 1; fibroblast growth factor homologous factor 1; myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor FGF-12b	273	2e-73
			Q92912	FGFC_HUMAN Fibroblast growth factor-12 (FGF-12) (Fibroblast growth factor homologous factor 1) (FHF-1) (Myocyte-activating factor)	273	2e-73
			AAB18913.1	fibroblast growth factor homologous factor 1	273	2e-73
			CAA94239.1	fibroblast growth factor 11	261	5e-70
			NP_004105.1	fibroblast growth factor 13, isoform 1A; fibroblast growth factor homologous factor 2	246	2e-65
			Q92913	FGFD_HUMAN Fibroblast growth factor-13 (FGF-13) (Fibroblast growth factor homologous factor 2) (FHF-2)	246	2e-65
			AAB18914.1	fibroblast growth factor homologous factor 2	246	2e-65
			AAD16400.1	fibroblast growth factor 13 isoform 1A	246	2e-65
			AAH12347.1	AAH12347 Unknown (protein for MGC:20109)	246	2e-65
			AAH34340.1	fibroblast growth factor 13	246	2e-65
			NP_004104.3	fibroblast growth factor 12 isoform 2; fibroblast growth factor homologous factor 1; myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor FGF-12b	223	2e-58
			JG0184	fibroblast growth factor - human	221	7e-58
			AAB18786.3	fibroblast growth factor	221	7e-58
			AAH22524.1	Unknown (protein for MGC:26659)	219	2e-57
			NP_378668.1	fibroblast growth factor 13 isoform 1B; fibroblast growth factor homologous factor 2	213	1e-55
			AAD16401.1	fibroblast growth factor 13 isoform 1B	213	1e-55



AK006553		U:(C-IR) 2.2						
BAB24650.1	Mm.59283	U:(C-D) 2.58 U:(IR-D) 2.72	XP_063839.1	hypothetical protein		398		e-110
			NP_689550.1	hypothetical protein FLJ32702		397		e-110
			BAB71401.1	unnamed protein product		397		e-110
NM_021370	Mm.8883	U:(C-IR) 2.19	XP_032835.1	similar to amiloride-sensitive sodium channel		776		0
NP_067345.1	9							
			CAB85607.1	amiloride-sensitive sodium channel		776		0
			AAB48981.1	sodium channel 2		218		2e-56
			NP_001086.2	amiloride-sensitive cation channel 2, neuronal isoform b; hBNAC2; Cation channel, amiloride-sensitive, neuronal, 2		218		2e-56
			AAC62935.1	proton-gated cation channel subunit		213		5e-55
			NP_064717.1	testis amiloride-sensitive cation channel 3, isoform b; testis sodium channel 1; proton-gated cation channel subunit; modulatory subunit of ASIC2a		211		3e-54
			AAF19818.1	AF195025_1 acid sensing ion channel 3 splice variant c		211		3e-54
			NP_004760.1	testis amiloride-sensitive cation channel 3, isoform a; testis sodium channel 1; proton-gated cation channel subunit; modulatory subunit of ASIC2a		211		3e-54
			AAC64188.1	proton-gated cation channel ASIC3		211		3e-54
			NP_064718.1	testis amiloride-sensitive cation channel 3, isoform c; testis sodium channel 1; proton-gated cation channel subunit; modulatory subunit of ASIC2a		211		3e-54
			AAF19817.1	AF195024_1 acid sensing ion channel 3 splice variant b		211		3e-54
			NP_001085.2	neuronal amiloride-sensitive cation channel 1; degenerin		206		1e-52
			Q16515	BNA1_HUMAN Amiloride-sensitive brain sodium channel BNaC1 (Amiloride-sensitive cation channel neuronal 1) (BNC1) (Degenerin channel MDEG)		206		1e-52
			AAC50498.1	degenerin channel MDEG		206		1e-52
			AAB49182.1	sodium channel 1		206		1e-52
			AAC50432.1	sodium channel 1		206		1e-52
			2211325A	Na channel		206		1e-52

			JE0091	testis sodium channel 1		203	5e-52
			BAA25897.1	sodium channel		203	5e-52
NM_019815	Mm.3509	U:(C-IR) 2.17	NP_057453.1	claudin 18		424	e-118
NP_062789.1	0	U:(C-D) 2.12					
			P56856	CLDI_HUMAN Claudin-18		424	e-118
			AAF26448.1	AF221069_1 Claudin-18		424	e-118
			AAL15637.1	AF349452_1 claudin-18A2.1		399	e-110
			NP_443192.1	retinoid binding protein 7; putative cellular retinol-binding protein CRBP IV		259	2e-69
NM_022020	Mm.4602	U:(C-IR) 2.17	Q96R05	RET7_HUMAN Retinol-binding protein IV, cellular (CRBP-IV) (Retinoid binding protein 7)		259	2e-69
NP_071303.1	3	U:(C-D) 2.04	AAK85409.1	retinoid binding protein 7		259	2e-69
			AAN61071.1	putative cellular retinol-binding protein CRBP IV		259	2e-69
			AAH33883.1	Similar to retinoid binding protein 7		212	3e-55
NM_007702							
NP_031728.1	Mm.449	U:(C-IR) 2.16	NP_001270.1	cell death-inducing DFFA-like effector a		340	3e-93
			O60543	CIDA_HUMAN Cell death activator CIDE-A (Cell death-inducing DFFA-like effector A)		340	3e-93
			AAC34987.1	cell death activator CIDE-A		340	3e-93
			AAH31896.1	Similar to cell death-inducing DFFA-like effector a		319	5e-87
NM_025639	Mm.2359	U:(C-IR) 2.16	NP_076958.1	hypothetical protein MGC861		293	2e-79
NP_079915.1	6						
			CAB77147.1	hypothetical protein		293	2e-79
			AAH00705.1	AAH00705 Unknown (protein for MGC:861)		293	2e-79
			AAH07495.1	AAH07495 hypothetical protein MGC861		293	2e-79

NM_025834 NP_080110.1	Mm.8079 8	U:(C-IR) 2.16	NP_003882.1	protein Z, vitamin K-dependent plasma glycoprotein	560	e-159
			P22891	PRTZ_HUMAN Vitamin K-dependent protein Z precursor	560	e-159
			AAA36500.1	protein Z	560	e-159
			BAA85763.1	protein Z	560	e-159
			AAL27631.1	AF440358_1 protein Z, vitamin K-dependent plasma glycoprotein	560	e-159
			KXHUZ	plasma protein Z precursor	550	e-156
			AAA36501.1	protein Z	550	e-156
			BAA85764.1	protein Z spliced variant	550	e-156
			AAA36499.1	protein Z	454	e-127
			AAA51984.1	coagulation factor X precursor	214	7e-55
			1205236A	coagulation factor X	214	7e-55
			AAA52490.1	factor X prepeptide	213	1e-54
			NP_000495.1	coagulation factor X precursor; Prothrombinase	213	1e-54
			P00742	FA10_HUMAN Coagulation factor X precursor (Stuart factor)	213	1e-54
			EXHU	coagulation factor Xa (EC 3.4.21.6) precursor	213	1e-54
			AAA52421.1	coagulation factor X	213	1e-54
			AAA52764.1	coagulation factor X	213	1e-54
			AAM19347.1	AF503510_1.coagulation factor X	213	1e-54
			CAA21954.1	F9 (coagulation factor IX (plasma thromboplastic component, Christmas disease, haemophilia B))	201	6e-51
			NP_000124.1	coagulation factor IX; Coagulation factor IX (plasma thromboplastic component); Factor 9; Factor IX; Christmas factor	201	6e-51
			AAA52023.1	coagulation factor IX precursor	201	6e-51
			AAA52763.1	factor IX (Christmas factor) precursor	201	6e-51
			AAM96188.1	coagulation factor IX (plasma thromboplastic component, Christmas disease, hemophilia B)	201	6e-51
			P00740	FA9_HUMAN Coagulation factor IX precursor (Christmas factor)	201	6e-51
			KFHU	coagulation factor IXa (EC 3.4.21.22) precursor	201	6e-51



				AAB59620.1	factor IX		201	6e-51
				AAA56822.1	factor IX		201	6e-51
				AAA98726.1	factor IX		199	3e-50
U16162				DAHUA1	procollagen-proline dioxygenase (EC 1.14.11.2) alpha chain precursor, splice form 1		1001	0
AAC52197.1	Mm.2212	U:(C-IR) 2.16						
				AAA59069.1	alpha-subunit of prolyl 4-hydroxylase		1001	0
				NP_000908.1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide I; procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide I		991	0
				AAA36534.1	prolyl 4-hydroxylase alpha subunit (EC 1.14.11.2)		991	0
				P13674	P4H1 HUMAN Prolyl 4-hydroxylase alpha-1 subunit precursor (4-PH alpha-1) (Procollagen-proline, 2-oxoglutarate 4-dioxygenase alpha-1 subunit)		982	0
				DAHUA2	procollagen-proline dioxygenase (EC 1.14.11.2) alpha chain precursor, splice form 2		982	0
				AAA59068.1	alpha-subunit of prolyl 4-hydroxylase		982	0
				AAH34998.1	Similar to procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide I		982	0
				AAA36535.1	prolyl 4-hydroxylase alpha subunit (EC 1.14.11.2)		971	0
				NP_004190.1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide II; prolyl 4-hydroxylase, alpha polypeptide, type 2; prolyl-4-hydroxylase, alpha polypeptide, type II		679	0
				O15460	P4H2 HUMAN Prolyl 4-hydroxylase alpha-2 subunit precursor (4-PH alpha-2) (Procollagen-proline, 2-oxoglutarate 4-dioxygenase alpha-2 subunit)		679	0
				AAB71339.1	prolyl 4-hydroxylase alpha (II) subunit		679	0
				CAC85689.1	Prolyl 4-hydroxylase alpha IIb subunit		679	0
				CAC85688.1	Prolyl 4-hydroxylase alpha IIa subunit		658	0
				AAH35813.1	Similar to procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide II		658	0
NM_013743	Mm.1028	U:(C-IR) 2.15		NP_002603.1	pyruvate dehydrogenase kinase, isoenzyme 4		764	0
NP_038771.1	3	U:(C-D) 2.04						

			Q16654	PDK4_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 4, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 4)	764	0
			AAC50669.1	pyruvate dehydrogenase kinase isoform 4	764	0
			AAC50670.1	pyruvate dehydrogenase kinase isoform 4	764	0
			AAB67048.1	pyruvate dehydrogenase kinase isoform 4	764	0
			AAH40239.1	pyruvate dehydrogenase kinase, isoenzyme 4	764	0
			NP_002601.1	pyruvate dehydrogenase kinase, isoenzyme 1	562	e-159
			Q15118	PDK1_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 1, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 1)	562	e-159
			I55465	[pyruvate dehydrogenase (lipoamide)] kinase (EC 2.7.1.99) 1	562	e-159
			AAC42009.1	pyruvate dehydrogenase kinase	562	e-159
			AAH39158.1	Similar to pyruvate dehydrogenase kinase, isoenzyme 1	562	e-159
			2203383A	pyruvate dehydrogenase kinase:ISOTYPE=1	562	e-159
			NP_002602.2	pyruvate dehydrogenase kinase, isoenzyme 2	556	e-157
			Q15119	PDK2_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 2, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 2)	556	e-157
			AAH05811.1	AAH05811 pyruvate dehydrogenase kinase, isoenzyme 2	556	e-157
			AAH40478.1	pyruvate dehydrogenase kinase, isoenzyme 2	556	e-157
			I70159	[pyruvate dehydrogenase (lipoamide)] kinase (EC 2.7.1.99) 2	554	e-157
			AAC42010.1	pyruvate dehydrogenase kinase	554	e-157
			2203383B	pyruvate dehydrogenase kinase:ISOTYPE=2	554	e-157
			NP_005382.1	pyruvate dehydrogenase kinase, isoenzyme 3	527	e-149
			Q15120	PDK3_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 3, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 3)	527	e-149
			I70160	[pyruvate dehydrogenase (lipoamide)] kinase (EC 2.7.1.99) 3	527	e-149
			AAC42011.1	pyruvate dehydrogenase kinase	527	e-149
			AAH15948.1	AAH15948 pyruvate dehydrogenase kinase, isoenzyme 3	527	e-149
			2203383C	pyruvate dehydrogenase kinase:ISOTYPE=3	527	e-149

NM_025806					NP_079105.1	hypothetical protein FLJ22662		870	0
NP_080082.1	Mm.3311	U:(C-IR) 2.15			BAB15442.1	unnamed protein product		870	0
					AAH00909.2	AAH00909 hypothetical protein FLJ22662		397	e-110
					XP_113725.2	similar to RIKEN cDNA 1300012G16		271	2e-72
					AAH30618.1	similar to RIKEN cDNA 1300012G16		271	2e-72
NM_008030		U:(C-IR) 2.14							
NP_032056.1	Mm.2900	U:(C-D) 2.22			P31513	FMO3_HUMAN Dimethylaniline monooxygenase [N-oxide forming] 3 (Hepatic flavin-containing monooxygenase 3) (FMO 3) (Dimethylaniline oxidase 3) (FMO II)		847	0
					AAC51932.1	flavin containing monooxygenase 3		847	0
						dJ127D3.1 (Hepatic Flavin-containing Monooxygenase 3 (Dimethylaniline Monooxygenase (N-Oxide forming) 3, EC1.14.13.8, Dimethylaniline Oxidase 3, FMO II, FMO 3))		847	0
					AAH32016.1	flavin containing monooxygenase 3		847	0
					NP_008825.2	flavin containing monooxygenase 3; Flavin-containing monooxygenase-3		846	0
					S51130	dimethylaniline monooxygenase (N-oxide-forming) (EC 1.14.13.8) 3		846	0
					CAA87632.1	flavin-containing monooxygenase 3 (FMO3)		846	0
					A38228	dimethylaniline monooxygenase (N-oxide-forming) (EC 1.14.13.8), hepatic 2		795	0
					AAA86284.1	flavoprotein		795	0
					CAA15909.1	dJ127D3.2 (Flavin-containing Monooxygenase family protein)		770	0
						FMO2_HUMAN Dimethylaniline monooxygenase [N-oxide forming] 2 (Pulmonary flavin-containing monooxygenase 2) (FMO 2) (Dimethylaniline oxidase 2) (FMO 1B1)			
					Q99518			610	e-174
					NP_002012.1	flavin containing monooxygenase 1; Flavin-containing monooxygenase 1 (fetal liver)		580	e-165
						FMO1_HUMAN DIMETHYLANILINE MONOOXYGENASE [N-OXIDE FORMING] 1 (FETAL HEPATIC FLAVIN-CONTAINING MONOOXYGENASE 1) (FMO 1) (DIMETHYLANILINE OXIDASE 1)			
					Q01740			580	e-165
					A40876	dimethylaniline monooxygenase (N-oxide-forming) (EC 1.14.13.8), hepatic 1		580	e-165
					AAA52457.1	flavin-containing monooxygenase		580	e-165

				NP_001451.1	flavin containing monoxygenase 2; Flavin-containing monoxygenase 2 (adult liver)	561	e-159
				CAA70462.1	flavin-containing monoxygenase 2	561	e-159
				CAA15910.1	dJ127D3.3 (Flavin-containing Monoxygenase 2)	561	e-159
				AAH05894.1	flavin containing monoxygenase 2	561	e-159
				P49326	FM05_HUMAN DIMETHYLANILINE MONOOXYGENASE [N-OXIDE FORMING] 5 (HEPATIC FLAVIN-CONTAINING MONOOXYGENASE 5) (FMO5) (DIMETHYLANILINE OXIDASE 5)	546	e-155
				S71618	dimethylaniline monoxygenase (N-oxide-forming) (EC 1.14.13.8) FMO5	546	e-155
				AAA67849.1	flavin-containing monoxygenase 5	546	e-155
				NP_001452.1	flavin containing monoxygenase 5	545	e-155
				S51131	flavin-containing monoxygenase 5 (FMO5)	545	e-155
				CAA87633.1	flavin-containing monoxygenase 5 (FMO5)	545	e-155
NM_011012 NP_035142.1	Mm.2991	U:(C-IR) 2.14		NP_000904.1	opiate receptor-like 1; opiate receptor-like 1; kappa3-related opiate receptor	573	e-163
				P41146	OPRX_HUMAN Nociceptin receptor (Orphanin FQ receptor) (Kappa-type 3 opiate receptor) (KOR-3)	573	e-163
				S43087	orphan opiate receptor ORL1	573	e-163
				CAA54386.1	ORL1	573	e-163
				AAA84913.1	orphan opiate receptor	573	e-163
				AAK11714.1	AF348323_1 nociceptin receptor	573	e-163
				AAH38433.1	opiate receptor-like 1	573	e-163
				AAL54890.1	AF126470_1 KOR-3D	558	e-159
				AAA96251.1	opiate receptor-like protein	509	e-144
				2201468A	opiate orphan receptor	509	e-144
				CAC17003.1	dJ1022E24.1 (opiate receptor-like protein 1 (OPRL1))	445	e-125
				CAC15482.1	dJ366F13.1 (opiate receptor mu 1)	296	4e-80
				P35372	OPRM_HUMAN Mu-type opiate receptor (MOR-1)	296	4e-80
				I56553	mu opiate receptor	296	4e-80
				AAA73958.1	opiate receptor	296	4e-80

			2108340A	mu opioid receptor		296	4e-80
			NP_000905.1	opioid receptor, mu 1		296	4e-80
			AAA20580.1	Mu opiate receptor		296	4e-80
			S65693	opioid receptor mu variant MOR1A		293	4e-79
			AAB60354.1	mu opioid receptor variant		293	4e-79
			AAN87342.1	DRG kappa 1 splice variant KOR 1A		285	8e-77
			P41143	OPRD_HUMAN Delta-type opioid receptor (DOR-1)		285	1e-76
			AAA83426.1	delta opiate receptor		285	1e-76
			CAA15671.1	dJ212P9.1		285	1e-76
NM_015750 NP_056565.1	Mm.4567 0	U:(C-IR) 2.14	NP_005374.1	sialidase 2; cytosolic sialidase; N-acetyl-alpha-neuraminidase 2; neuraminidase 2		539	e-153
			Q9Y3R4	NER2_HUMAN Sialidase 2 (Cytosolic sialidase) (N-acetyl-alpha-neuraminidase 2)		539	e-153
			CAB41449.1	neuraminidase; sialidase		539	e-153
			NP_006647.2	sialidase 3; neuraminidase 3; ganglioside sialidase; N-acetyl-alpha-neuraminidase 3		267	4e-71
			CAB96131.1	Nuraminidase		267	4e-71
			Q9UQ49	NER3_HUMAN Sialidase 3 (Membrane sialidase) (Ganglioside sialidase) (N-acetyl-alpha-neuraminidase 3)		264	3e-70
			BAA82611.1	ganglioside sialidase		264	3e-70
			CAC81904.1	sialidase		231	2e-60
			NP_542779.2	sialidase		231	3e-60
NM_031389 NP_113566.1	Mm.8479 2	U:(C-IR) 2.14	XP_085972.4	similar to PYRIN-containing APAF1-like protein 4; PAAD and NACHT-containing protein 2; ribonuclease inhibitor 2		758	0
			NP_604393.1	PYRIN-containing APAF1-like protein 4; PAAD and NACHT-containing protein 2; ribonuclease inhibitor 2		758	0
			Q96MN2	NAL4_HUMAN NACHT-, LRR- and PYD-containing protein 4 (PAAD and NACHT-containing protein 2) (PYRIN-containing APAF1-like protein 4) (Ribonuclease inhibitor 2)		758	0
			AAL35293.1	AF442488_1 NALP4		758	0
			AAL68396.1	PAAD and NACHT-containing protein 2		758	0

				AAI87104.1	AF479747_1 PYRIN-containing APAF1-like protein 4	758	0
				BAB71254.1	unnamed protein product	758	0
				AAI88672.1	AF482706_1 ribonuclease inhibitor 2	749	0
				XP_062261.4	similar to PYRIN-containing APAF1-like Protein 7	495	e-139
				NP_659444.1	PYRIN-containing APAF1-like protein 6	427	e-119
				P59045	PYA6_HUMAN PYRIN-containing APAF1-like protein 6	427	e-119
				AAM14632.1	PYRIN-containing APAF1-like protein 6	427	e-119
				AAH34730.1	PYRIN-containing APAF1-like protein 6	427	e-119
				AAH16443.1	AAH16443 Unknown (protein for IMAGE:3448931)	391	e-108
				AAI78632.1	AF468522_1 NALP3 long isoform	379	e-104
				NP_004886.2	cold autoimmune syndrome 1; chromosome 1 open reading frame 7; angiotensin/vasopressin receptor AII/AVP-like; cryopyrin; PYRIN-containing APAF1-like protein 1	378	e-104
				Q96P20	CIS1_HUMAN Cold autoimmune syndrome 1 protein (Cryopyrin) (NACHT-, LRR- and PYD-containing protein 3) (PYRIN-containing APAF1-like protein 1) (Angiotensin/vasopressin receptor AII/AVP-like)	378	e-104
				AAI33908.1	AF410477_1 cryopyrin	378	e-104
				AAI12497.1	cryopyrin	378	e-104
				AAI65136.1	AF420469_1 PYRIN-containing APAF1-like protein 1	378	e-104
				XP_064988.5	similar to PYRIN-containing APAF1-like protein 4; PAAD and NACHT-containing protein 2; ribonuclease inhibitor 2	367	e-101
NM_025621 NP_079897.1	Mm.1442 59	U:(C-IR) 2.11		XP_088993.1	similar to RIKEN cDNA 2310050C09	229	5e-60
NM_011377 NP_035507.1	Mm.4775	U:(C-IR) 2.09		NP_005060.1	single-minded (Drosophila) homolog 2 long isoform; human transcription factor SIM2, homolog of the Drosophila single-minded gene SIM1	939	0
				Q14190	SIM2_HUMAN Single-minded homolog 2	939	0
				AAB62396.1	transcription factor SIM2 long form	939	0
				BAA89433.1	single-minded 2 protein	939	0

			NP_033664.1	single-minded (Drosophila) homolog 2 short isoform; human transcription factor SIM2, homolog of the Drosophila single-minded gene SIM1	849	0
			AAB62397.1	transcription factor SIM2 short form	849	0
			CAA05055.1	human SIM2	729	0
			NP_005059.2	single-minded (Drosophila) homolog 1; Single-minded, drosophila, homolog of, 1	634	0
			P81133	SIM1_HUMAN Single-minded homolog 1	629	e-180
			AAB62395.1	hSIM1	629	e-180
			A58520	single-minded gene 2 protein	462	e-129
			BAA12919.1	Sim	461	e-129
			NP_071406.1	basic-helix-loop-helix-PAS protein	295	3e-79
			AAG35180.1	AF164438_1 basic-helix-loop-helix-PAS protein	295	3e-79
			BAB21221.1	NPAS3 (MOP6)	295	5e-79
			BAC53756.1	NPAS3	295	5e-79
AF319951			AAM73657.1	solute carrier family 12 member 8	1011	0
AAL37178.1	Mm.35253	U:(C-IR) 2.08	AAK94307.1	solute carrier family 12 member 8	766	0
			AAH20506.1	hypothetical protein FLJ23188	370	e-102
			NP_078904.1	solute carrier family 12 (potassium/chloride transporters), member 8; solute carrier family 12 (sodium/potassium/chloride transporters), member 8	369	e-101
			BAB15571.1	unnamed protein product	369	e-101
			NP_001037.1	solute carrier family 12 (sodium/potassium/chloride transporters), member 2; Solute carrier family 12 (sodium/potassium/chloride transporters)	229	2e-59
			P55011	S122_HUMAN Solute carrier family 12 member 2 (Bumetanide-sensitive	229	2e-59
			A57187	bumetanide-sensitive Na-K-Cl cotransporter	229	2e-59
			AAC50561.1	bumetanide-sensitive Na-K-Cl cotransporter	229	2e-59
			AAH33003.1	Similar to solute carrier family 12 (sodium/potassium/chloride	229	2e-59
			NP_000329.1	sodium potassium chloride cotransporter 2; Solute carrier family 12	223	1e-57
			Q13621	S121_HUMAN Solute carrier family 12 member 1 (Bumetanide-sensitive	223	1e-57
			AAB07364.1	bumetanide-sensitive Na-K-2Cl cotransporter	223	1e-57

				P55017	SI23_HUMAN Solute carrier family 12 member 3 (Thiazide-sensitive sodium-chloride	201	4e-51
				NP_000330.1	solute carrier family 12 (sodium/chloride transporters), member 3; Solute carrier family 12 (sodium/potassium/chloride transporters),	201	4e-51
				AAC50355.1	thiazide-sensitive Na-Cl	201	4e-51
				G01202	NaCl electroneutral Thiazide-sensitive cotransporter	201	5e-51
				CAA62613.1	NaCl electroneutral Thiazide-sensitive cotransporter	201	5e-51
NM_008074							
NP_032100.1	Mm.1345	U:(C-IR) 2.08		NP_150092.1	gamma-aminobutyric acid (GABA) A receptor, gamma 3	841	0
				AAB39369.1	GABAA receptor gamma 3 subunit	841	0
				Q99928	GAC3_HUMAN Gamma-aminobutyric-acid receptor gamma-3 subunit precursor (GABA(A) receptor)	838	0
				AAF99698.1	GABAA receptor gamma 3 subunit	838	0
				AAF63215.1	GABAA receptor gamma 3 subunit	836	0
				AAD50273.1	gamma-aminobutyric acid A receptor gamma 2	588	e-167
				NP_000807.1	gamma-aminobutyric acid A receptor, gamma 2 precursor	584	e-166
				P18507	GAC2_HUMAN Gamma-aminobutyric-acid receptor gamma-2 subunit precursor (GABA(A) receptor)	584	e-166
				S03905	gamma-aminobutyric acid/benzodiazepine receptor gamma-2 chain precursor	584	e-166
				CAA33437.1	GABA-A receptor gamma 2 subunit	584	e-166
				1506443A	GABAA receptor gamma2	584	e-166
				AAH31087.1	similar to GAMMA-AMINOBTYRIC-ACID RECEPTOR GAMMA-1 SUBUNIT PRECURSOR (GABA(A) RECEPTOR)	576	e-164
				XP_094080.1	similar to Gamma-aminobutyric-acid receptor gamma-1 subunit precursor (GABA(A) receptor) [Homo sapiens]	576	e-164
				NP_004952.1	gamma-aminobutyric acid (GABA) A receptor, epsilon, isoform 1 precursor	378	e-104
				AAB49284.1	GABA-A receptor epsilon subunit	378	e-104
				P78334	GAE_HUMAN Gamma-aminobutyric-acid receptor epsilon subunit precursor (GABA(A) receptor)	378	e-104



				CAA70904.1	GABA receptor epsilon subunit		378	e-104
				AAB94645.1	GABA-A receptor epsilon subunit		378	e-104
				CAA70903.1	GABRE		374	e-103
NM_010899	Mm.1168	U:(C-IR)		Q13469	NFC2_HUMAN Nuclear factor of activated T-cells, cytoplasmic 2 (T cell transcription factor NFAT1) (NFAT pre-existing subunit)(NF-ATp)		1522	0
NP_035029.1	02	2.08		AAC50887.1	transcription factor NFAT1 isoform C		1522	0
				NP_036472.1	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2; nuclear factor of activated T-cells, cytoplasmic 2		1487	0
				G02326	transcription factor NFAT1 isoform B - human		1487	0
				AAC50886.1	transcription factor NFAT1 isoform B		1487	0
				CAC00528.1	dJ994O24.1 (nuclear factor of activated T-cells, cytoplasmic 2 (isoforms B and C))		835	0
				CAB54871.1	dJ1009H6.1.2 (nuclear factor of activated T-cells, cytoplasmic 2, isoform C)		649	0
				CAC00529.1	dJ1009H6.1.1 (nuclear factor of activated T-cells, cytoplasmic 2, isoform B)		615	e-175
				1A02	N Chain N, Structure Of The Dna Binding Domains Of Nfat, Fos And Jun Bound To Dna		567	e-161
				AAD00451.1	transcription factor		551	e-156
				O95644	NFC1_HUMAN Nuclear factor of activated T-cells, cytoplasmic 1 (NFAT transcription complex cytosolic component) (NF-ATc1) (NF-ATc)		550	e-156
				AAC50869.1	nuclear factor of activated T cells		523	e-148
				NP_006153.2	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1; nuclear factor of activated T-cells, cytoplasmic 1		521	e-147
				AAD00450.1	transcription factor		521	e-147
				NP_037504.1	cysteine knot superfamily 1, BMP antagonist 1; gremlin		311	2e-84
NM_011824	Mm.3046	U:(C-IR)						
NP_035954.1	5	2.07						
				AAC39725.1	gremlin		311	2e-84
				BAA84462.1	gremlin homologue		311	2e-84
				AAF06677.1	gremlin		311	2e-84
				AAG23891.1	AF154054 1 DRM		311	2e-84

				BAC04620.1	unnamed protein product		254	3e-67
				BAC04643.1	unnamed protein product		253	8e-67
AF193796	Mm.20706	U:(C-IR)		XP_006804.2	similar to Homeobox protein Hox-C13 (Hox-3G)			
AAL09298.1	2	2.07		NP_059106.2	homeo box C13; homeobox protein Hox-C13; homeo box 3G		505	e-142
				P31276	HXCD_HUMAN Homeobox protein Hox-C13 (Hox-3G)		505	e-142
				AAF73439.1	HOXC13		505	e-142
				AAH02754.1	homeo box C13		505	e-142
				AAF67760.1	homeoprotein C13		504	e-142
				BAB14786.1	unnamed protein product		280	7e-75
				P31271	HXAD_HUMAN Homeobox protein Hox-A13		218	4e-56
				AAC50993.1	transcription factor HOXA13		218	4e-56
				NP_000513.2	homeobox protein A13; homeobox protein HOXA13; homeo box 1J; transcription factor HOXA13		218	4e-56
				NP_000514.1	homeo box D13; homeo box 4I; homeobox protein Hox-D13		216	2e-55
				P35453	HXDD_HUMAN Homeobox protein Hox-D13 (Hox-4I)		216	2e-55
				AAC51635.1	HOXD13		216	2e-55
				BAA95352.1	homeobox transcription factor		216	2e-55
NM_008152								
NP_032178.1	Mm.2840	U:(C-IR)		XP_007392.1	similar to G protein-coupled receptor 65; T-cell death-associated gene 8		527	e-149
				AAH35633.1	similar to G protein-coupled receptor		527	e-149
				NP_003599.1	G protein-coupled receptor 65; T-cell death-associated gene 8		521	e-147
				AAC31794.1	T cell-death associated protein		521	e-147
				S68207	G protein-coupled receptor 6C.1		196	8e-50
				AAA79061.1	G protein-coupled receptor		196	8e-50
				2124311B	G protein-coupled receptor		196	8e-50

				NP_005273.1	G protein-coupled receptor 4		196	8e-50
				XP_009140.1	similar to Probable G protein-coupled receptor GPR4 (GPR19)		196	8e-50
				P46093	GPR4_HUMAN Probable G protein-coupled receptor GPR4 (GPR19)		196	8e-50
				A57641	G protein-coupled receptor 4		196	8e-50
				AAA98457.1	G protein-coupled receptor		196	8e-50
				I53033	G protein-coupled receptor		196	8e-50
				AAA63180.1	G protein-coupled receptor		196	8e-50
NM_008324								
NP_032350.1	Mm.392	U:(C-IR) 2.07		NP_002155.1	indoleamine-pyrrole 2,3-dioxygenase; Indoleamine 2,3-dioxygenase; indole 2,3-dioxygenase		499	e-141
				P14902	I23O_HUMAN Indoleamine 2,3-dioxygenase (IDO) (Indoleamine-pyrrole 2,3-dioxygenase)		499	e-141
				PC1161	indoleamine-pyrrole 2,3-dioxygenase (EC 1.13.11.42)		499	e-141
				CAA35663.1	indoleamine 2,3-dioxygenase		499	e-141
				AAA36081.1	indoleamine 2,3-dioxygenase (IDO) (EC 1.13.11.17)		499	e-141
				AAH27882.1	indoleamine-pyrrole 2,3-dioxygenase		499	e-141
				XP_095645.4	similar to indoleamine 2,3-dioxygenase		313	4e-85
NM_009827								
NP_033957.1	Mm.3521	U:(C-IR) 2.07		NP_000721.1	cholecystokinin A receptor		693	0
				P32238	CKKR_HUMAN Cholecystokinin type A receptor (CCK-A receptor) (CCK-AR)		693	0
				JN0692	cholecystokinin type A receptor		693	0
				AAA35659.1	cholecystokinin A receptor		693	0
				AAA02819.1	cholecystokinin A receptor		693	0
				AAA91123.1	cholecystokinin type A receptor		693	0
				BAA90879.1	cholecystokinin type-A receptor		693	0
				2118221A	cholecystokinin A receptor		679	0
				P32239	GASR_HUMAN Gastrin/cholecystokinin type B receptor (CCK-B receptor) (CCK-BR)		350	8e-96

			A47430	gastrin/cholecystokinin receptor B, short splice form	350	8e-96
			AAA35660.1	cholecystokinin receptor	350	8e-96
			AAA35657.1	cholecystokinin-B/gastrin receptor	350	8e-96
			AAC37528.1	gastrin receptor	350	8e-96
			BAA02564.1	cholecystokinin receptor	350	8e-96
			AAH00740.1	AAH00740 cholecystokinin B receptor	350	8e-96
			AAA91831.1	cholecystokinin B receptor	348	2e-95
			AAB30766.2	cholecystokinin B receptor	348	2e-95
			BAA04759.1	cholecystokinin-B receptor/gastrin receptor	348	4e-95
			AAC27510.1	gastrin\cholecystokinin brain receptor	345	3e-94
			AAK38351.1	CCK-B/gastrin receptor variant	243	1e-63
			AAN32829	AF441129_1 cholecystokinin-C receptor	243	1e-63
			NP_000722.2	cholecystokinin B receptor	241	5e-63
			AAF67174.1	AF239668_1 CCK-B/gastrin receptor	241	5e-63
NM_013920	Mm.4198	U:(C-IR)	JC6095	hepatocyte nuclear factor 4 gamma chain	749	0
NP_038948.1	5	2.07				
			2208436B	hepatocyte nuclear factor 4	749	0
			NP_004124.2	hepatocyte nuclear factor 4, gamma	739	0
			CAA89990.2	hepatocyte nuclear factor 4 gamma (HNF4gamma)	739	0
			Q14541	HN4G_HUMAN Hepatocyte nuclear factor 4-gamma (HNF-4-gamma)	738	0
			AAF00110.1	hepatocyte nuclear factor 4 gamma	738	0
			CAA61133.1	Hepatocyte nuclear factor 4A	582	e-166
			AAB48082.1	hepatocyte nuclear factor 4-alpha	579	e-165
			NP_000448.2	hepatocyte nuclear factor 4, alpha; transcription factor-14; hepatic nuclear factor 4, alpha	579	e-165
			JC6096	hepatocyte nuclear factor 4 alpha2 chain	579	e-165
			CAA89989.1	hepatocyte nuclear factor 4 alpha (HNF4alpha4)	579	e-165
			2208436A	hepatocyte nuclear factor 4:ISOTYPE=alpha	579	e-165

				CAC01303.1	dJ1013A22.1 (hepatocyte nuclear factor 4, alpha)		578	e-165
				P41235	HN4A_HUMAN Hepatocyte nuclear factor 4-alpha (HNF-4-alpha) (Transcription factor HNF-4) (Transcription factor 14)		578	e-165
				CAA54248.1	hepatocyte nuclear factor 4		576	e-164
				JC4937	hepatocyte nuclear factor 4, splice form B		575	e-164
				CAA61134.1	Hepatocyte nuclear factor 4B		575	e-164
NM_020028	Mm.2325	U:(C-IR)		NP_004711.2	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4; G protein-coupled receptor; lysophosphatidic acid receptor EDG4; LPA receptor EDG4		470	e-132
NP_064412.1	3	2.07		Q9HBW0	EDG4_HUMAN Lysophosphatidic acid receptor Edg-4 (LPA receptor 2) (LPA-2)		470	e-132
				AAB61528.1	R33799_1		470	e-132
				AAF43409.1	AF233092_1 lysophosphatidic acid G protein-coupled receptor 4		470	e-132
				AAH25695.1	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4		470	e-132
				AAG28521.1	AF197929_1 lysophosphatidic acid receptor EDG4		468	e-131
				AAC27728.1	G protein-coupled receptor Edg-4		463	e-130
				NP_001392.2	lysophosphatidic acid receptor EDG2; ventricular zone gene 1; LPA receptor EDG2		255	2e-67
				NP_476500.1	lysophosphatidic acid receptor EDG2; ventricular zone gene 1; LPA receptor EDG2		255	2e-67
				Q92633	EDG2_HUMAN Lysophosphatidic acid receptor Edg-2 (LPA receptor 1) (LPA-1)		255	2e-67
				CAA70686.1	G protein-coupled receptor Edg-2		255	2e-67
				AAC00530.1	Edg-2 receptor		255	2e-67
				AAH30615.1	Unknown (protein for MGC:33156)		255	2e-67
				AAH36034.1	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 2		255	2e-67
				JC5293	lysophosphatidic acid receptor		255	2e-67
				AAC51139.1	lysophosphatidic acid receptor homolog		255	2e-67
				CAA70687.1	G protein-coupled receptor Edg-2		255	2e-67
				NP_036284.1	endothelial cell differentiation gene 7; calcium-mobilizing lysophosphatidic acid receptor LP-A3; LPA receptor EDG7		225	3e-58
				Q9UBY5	EDG7_HUMAN Lysophosphatidic acid receptor Edg-7 (LPA receptor 3) (LPA-3)		225	3e-58
				AAD56311.1	AF127138_1 lysophosphatidic acid G protein-coupled receptor		225	3e-58

				AAF00530.1	AF186380_1 calcium-mobilizing lysophosphatidic acid receptor LP-A3/Edg-7	225	3e-58
				AAF91291.1	G-protein coupled receptor EDG-7	222	2e-57
AK015988							
XP_129281.1	Mm.40665	U:(C-IR) 2.06		NP_079065.1	hypothetical protein FLJ22529	137	5e-89
				BAB15385.1	unnamed protein product	137	5e-89
NM_009565		U:(C-IR) 2.05					
NP_033591.1	Mm.17068 4	U:(C-D) 2.13		AAH12070.1	Similar to kruppel-related zinc finger protein hcKrox	593	e-170
				NP_056956.1	kruppel-related zinc finger protein hcKrox	592	e-170
				AAC51847.1	kruppel-related zinc finger protein hcKrox	592	e-170
				XP_113971.1	similar to HIV-1 inducer of short transcripts binding protein	206	9e-53
				NP_056982.1	HIV-1 inducer of short transcripts binding protein	205	3e-52
				AAC72973.1	HIV-1 inducer of short transcripts binding protein	205	3e-52
NM_008158							
NP_032184.1	Mm.35009	U:(C-IR) 2.05		NP_061844.1	G protein-coupled receptor 27; super conserved receptor expressed in brain 1	453	e-127
				Q9NS67	GP27_HUMAN Probable G protein-coupled receptor GPR27 (Super conserved receptor expressed in brain 1)	453	e-127
				JC7287	G-protein coupled receptor, SREB1	453	e-127
				BAA96645.1	SREB1	453	e-127
				AAH30577.1	similar to G protein-coupled receptor 85	249	5e-66
				NP_061843.1	G protein-coupled receptor 85; super conserved receptor expressed in brain 2	248	2e-65
				Q9NPD1	GP85_HUMAN Probable G protein-coupled receptor GPR85 (Super conserved receptor expressed in brain 2) (PKrCx1)	248	2e-65
				T47131	G-protein coupled receptor, SREB2	248	2e-65
				CAB82307.1	hypothetical protein	248	2e-65
				BAA96646.1	SREB2	248	2e-65
				AAF79956.1	AF250237_1 orphan G protein-coupled receptor 85	248	2e-65

				BAC05911.1	seven transmembrane helix receptor	248	2e-65
				NP_061842.1	super conserved receptor expressed in brain 3	233	3e-61
				Q9NS66	SRB3_HUMAN Super conserved receptor expressed in brain 3	233	3e-61
				JC7289	G-protein coupled receptor, SREB3	233	3e-61
				BAA96647.1	SREB3	233	3e-61
				AAH09861.1	AAH09861 super conserved receptor expressed in brain 3	233	3e-61
NM_019513 NP_062386.1	Mm.1170 15	U:(C-IR) 2.05		NP_009151.1	carbonic anhydrase VB, mitochondrial precursor; carbonic dehydratase	605	e-173
				Q9Y2D0	CA5B_HUMAN Carbonic anhydrase VB, mitochondrial precursor (Carbonate dehydratase VB) (CA-VB)	605	e-173
				BAA76671.1	carbonic anhydrase VB	605	e-173
				AAH28142.1	carbonic anhydrase VB, mitochondrial	605	e-173
				NP_001730.1	carbonic anhydrase VA, mitochondrial precursor; carbonic anhydrase V, mitochondrial; carbonic dehydratase	384	e-106
				P35218	CAH5_HUMAN Carbonic anhydrase VA, mitochondrial precursor (Carbonate dehydratase VA) (CA-VA)	384	e-106
				CRHU5	carbonate dehydratase (EC 4.2.1.1) V precursor [validated]	384	e-106
				AAA02890.1	carbonic anhydrase V	384	e-106
				AAB47048.1	carbonic anhydrase V; CA V	384	e-106
				AAC99806.1	carbonic anhydrase V	384	e-106
				IUGD	Human Carbonic Anhydrase Ii[hcai] (E.C.4.2.1.1) Mutant With Ala 65 Replaced By Ser (A65s)	286	4e-77
				IUGG	Human Carbonic Anhydrase Ii[hcai] (E.C.4.2.1.1) Mutant With Ala 65 Replaced By Ser (A65s) - Orthorhombic Form	286	4e-77
				IUGF	Human Carbonic Anhydrase Ii [hcai] (E.C.4.2.1.1) Mutant With Ala 65 Replaced By Thr (A65t)	285	9e-77
				1G52	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N-[(2,3-Difluorophenyl)methyl]-Benzamide	285	9e-77
				1G54	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N-[(2,3,4,5,6-Pentafluorophenyl)methyl]-Benzamide	285	9e-77

			118Z	A Chain A, Carbonic Anhydrase Ii Complexed With Al-6629 2h-Thieno[3,2-E]-1,2-Thiazine-6-Sulfonamide, 2-(3-Methoxyphenyl)-3-(4-Morpholinyl)-, 1,1-Dioxide	285	9e-77
			11F4	A Chain A, Carbonic Anhydrase Ii Complexed With 4-Fluorobenzenesulfonamide	285	9e-77
			1G53	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N-[(2,6-Difluorophenyl)methyl]-Benzamide	285	9e-77
			11F8	A Chain A, Carbonic Anhydrase Ii Complexed With (S)-N-(3-Indol-1-Yl-2-Methyl-Propyl)-4-Sulfamoyl-Benzamide	285	9e-77
			11F7	A Chain A, Carbonic Anhydrase Ii Complexed With (R)-N-(3-Indol-1-Yl-2-Methyl-Propyl)-4-Sulfamoyl-Benzamide	285	9e-77
			1190	A Chain A, Carbonic Anhydrase Ii Complexed With Al-8520 2h-Thieno[3,2-E]-1,2-Thiazine-6-Sulfonamide, 4-Amino-3,4-Dihydro-2-(3-Methoxypropyl)-, 1,1-Dioxide, ®	285	9e-77
			1191	A Chain A, Carbonic Anhydrase Ii Complexed With Al-6619 2h-Thieno[3,2-E]-1,2-Thiazine-6-Sulfonamide, 2-(3-Hydroxyphenyl)-3-(4-Morpholinyl)-, 1,1-Dioxide	285	9e-77
			11F5	A Chain A, Carbonic Anhydrase Ii Complexed With 2,6-Difluorobenzenesulfonamide	285	9e-77
			11F9	A Chain A, Carbonic Anhydrase Ii Complexed With N-[2-(1h-Indol-5-Yl)-Butyl]-4-Sulfamoyl-Benzamide	285	9e-77
			1G1D	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N-[(2-Fluorophenyl)methyl]-Benzamide	285	9e-77
			11F6	A Chain A, Carbonic Anhydrase Ii Complexed With 3,5-Difluorobenzenesulfonamide	285	9e-77
			1AM6	Carbonic Anhydrase Ii Inhibitor: Acetohydroxamate	285	9e-77
			1F2W	A Chain A, The Mechanism Of Cyanamide Hydration Catalyzed By Carbonic Anhydrase Ii Revealed By Cryogenic X-Ray Diffraction	285	9e-77
			1OKM	Carbonic Anhydrase Ii Complex With The 10km Inhibitor 4-Sulfonamide-[1-(4-Aminobutane)]benzamide	285	9e-77
			1BN1	Carbonic Anhydrase Ii Inhibitor	285	9e-77
			1BN4	Carbonic Anhydrase Ii Inhibitor	285	9e-77
			1BN3	Carbonic Anhydrase Ii Inhibitor	285	9e-77
			1BNN	Carbonic Anhydrase Ii Inhibitor	285	9e-77



			1BNV	Carbonic Anhydrase Ii Inhibitor	285	9e-77
			1BNM	Carbonic Anhydrase Ii Inhibitor	285	9e-77
			1CIL	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complexed With The Inhibitor Ets	285	9e-77
			2CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA ID) (E.C.4.2.1.1) Complex With Thiocyanate Ion	285	9e-77
			3CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA ID) (E.C.4.2.1.1) Complex With 3-Mercuri-4-Aminobenzenesulfonamide (AMS).	285	9e-77
			1CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA ID) (E.C.4.2.1.1)	285	9e-77
			1BNT	Carbonic Anhydrase Ii Inhibitor	285	9e-77
			1BNU	Carbonic Anhydrase Ii Inhibitor	285	9e-77
			1A42	Human Carbonic Anhydrase Ii Complexed With Brinzolamide	285	9e-77
			1BNW	Carbonic Anhydrase Ii Inhibitor	285	9e-77
			1BNQ	Carbonic Anhydrase Ii Inhibitor	285	9e-77
			1OKN	Carbonic Anhydrase Ii Complex With The 1okn Inhibitor 4-Sulfonamide-[1-(4-N-(5-Fluorescein Thiourea)butane)]	285	9e-77
			1OKL	Carbonic Anhydrase Ii Complex With The 1okl Inhibitor 5-Dimethylamino-Naphthalene-1-Sulfonamide	285	9e-77
			1CRA	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complex With 1,2,4-Triazole	285	9e-77
			1CAO	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complex With Hydrogen Sulfide	285	9e-77
			2CBA	Carbonic Anhydrase Ii (E.C.4.2.1.1) (50 Mm Tris, 3 M Ammonium Sulfate, Ph 7.8)	285	9e-77
			2CBD	Carbonic Anhydrase Ii (E.C.4.2.1.1) (2.4 M Ammonium Sulfate, 0.3 M Sodium Bisulfite, Ph 7.3)	285	9e-77
			2CBB	Carbonic Anhydrase Ii (E.C.4.2.1.1) (80 Mm Sodium Citrate, 2.4 M Ammonium Sulfate, Ph 6.0)	285	9e-77
			1RAY	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complex With Azide	285	9e-77
			1RZB	Carbonic Anhydrase Ii (E.C.4.2.1.1) With Zinc Replaced By By Cobalt(Ii) At Ph 6.0	285	9e-77
			2CBE	Carbonic Anhydrase Ii (E.C.4.2.1.1) (50 Mm Tris, 3 M Ammonium Sulfate, 2mm Dipicolinate, Ph 7.8)	285	9e-77
			2CBC	Carbonic Anhydrase Ii (E.C.4.2.1.1) (50 Mm Tris, 3 M Ammonium Sulfate, 0.2 Formate, Ph 7.6)	285	9e-77

		1CAH	Carbonic Anhydrase II (E.C.4.2.1.1) (Native Zinc Replaced By Cobalt) Complex With Bicarbonate	285	9e-77
		1RZC	Carbonic Anhydrase II (E.C.4.2.1.1) With Zinc Replaced By Copper(II)	285	9e-77
		1BCD	Carbonic Anhydrase II (E.C.4.2.1.1) Complex With Trifluoromethane Sulphonamide	285	9e-77
		1RAZ	Carbonic Anhydrase II (E.C.4.2.1.1) Complex With Bromide	285	9e-77
		1RZA	Carbonic Anhydrase II (E.C.4.2.1.1) With Zinc Replaced By Cobalt(II)	285	9e-77
		1RZD	Carbonic Anhydrase II (E.C.4.2.1.1) With Zinc Replaced By Manganese(II)	285	9e-77
		1RZE	Carbonic Anhydrase II (E.C.4.2.1.1) With Zinc Replaced By Nickel(II)	285	9e-77
		1CAY	Carbonic Anhydrase II (E.C.4.2.1.1) Complex With Acetate	285	9e-77
		5CAC	Carbonic Anhydrase Form C (E.C.4.2.1.1) Complex With Hydrogen Sulfite	285	9e-77
		4CAC	Carbonic Anhydrase Form C (E.C.4.2.1.1) (Ph 6)	285	9e-77
		1BV3	A Chain A, Human Carbonic Anhydrase II Complexed With Urea	285	9e-77
		1AVN	Human Carbonic Anhydrase II Complexed With The Histamine Activator	285	9e-77
		1LZV	A Chain A, Site-Specific Mutant (Tyr7 Replaced With His) Of Human Carbonic Anhydrase II	285	9e-77
		NP_000058.1	carbonic anhydrase II; carbonate dehydratase II; carbonic dehydratase; carbonic anhydrase B	285	9e-77
		P00918	CAH2_HUMAN Carbonic anhydrase II (Carbonate dehydratase II) (CA-II) (Carbonic anhydrase C)	285	9e-77
		CRHU2	carbonate dehydratase (EC 4.2.1.1) II [validated]	285	9e-77
		1EOU	A Chain A, Crystal Structure Of Human Carbonic Anhydrase II Complexed With An Anticonvulsant Sugar Sulfamate	285	9e-77
		1CNX	Mol_id: 1; Molecule: Carbonic Anhydrase II; Chain: Null; Synonym: Carbonate Dehydratase, Hca II; Ec: 4.2.1.1; Heterogen: Benzenesulfonamide	285	9e-77
		1CNW	Mol_id: 1; Molecule: Carbonic Anhydrase II; Chain: Null; Synonym: Carbonate Dehydratase, Hca II; Ec: 4.2.1.1; Heterogen: Ethylaminocarbonylbenzenesulfonamide	285	9e-77
		1CNY	Mol_id: 1; Molecule: Carbonic Anhydrase II; Chain: Null; Synonym: Carbonate Dehydratase, Hca II; Ec: 4.2.1.1; Heterogen: Aminocarbonylbenzenesulfonamide	285	9e-77
		4CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1)	285	9e-77
		1CA3	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1) (pH 5.7)	285	9e-77

			1HCA	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1) (pH 6.5)	285	9e-77
			CAA68426.1	carbonic anhydrase II (AA 1-260)	285	9e-77
			AAA51908.1	carbonic anhydrase II	285	9e-77
			AAA51909.1	carbonic anhydrase II	285	9e-77
			AAA51911.1	carbonic anhydrase II	285	9e-77
			1UGB	Human Carbonic Anhydrase II[hcai] (E.C.4.2.1.1) Mutant With Ala 65 Replaced By Gly (A65g)	285	1e-76
			1LG5	A Chain A, Crystal Structure Analysis Of The Hca Ii Mutant T199p In Complex With Beta-Mercaptoethanol	285	1e-76
			1LG6	A Chain A, Crystal Structure Analysis Of Hca Ii Mutant T199p In Complex With Thiocyanate	285	1e-76
			1LGD	A Chain A, Crystal Structure Analysis Of Hca Ii Mutant T199p In Complex With Bicarbonate	285	1e-76
NM_008890						
NP_032916.1	Mm.57030	U:(C-IR) 2.04	NP_002677.1	phenylethanolamine N-methyltransferase	462	e-130
			P11086	PNMT HUMAN Phenylethanolamine N-methyltransferase (PNMTase) (Noradrenaline N-methyltransferase)	462	e-130
			A28171	phenylethanolamine N-methyltransferase (EC 2.1.1.28)	462	e-130
			1HNN	B Chain B, Crystal Structure Of Human Pnmt Complexed With Sk&f 29661 And Adohcy(Sah)	462	e-130
			1HNN	A Chain A, Crystal Structure Of Human Pnmt Complexed With Sk&f 29661 And Adohcy(Sah)	462	e-130
			AAA60130.1	phenylethanolamine N-methyltransferase	462	e-130
			CAA36944.1	phenylethanolamine n-methyltransferase	462	e-130
			AAH37246.1	phenylethanolamine N-methyltransferase	462	e-130
			AAA60131.1	phenylethanolamine N-methyltransferase	461	e-130
NM_008985						
NP_033011.1	Mm.2902	U:(C-IR) 2.04	NP_002837.1	protein tyrosine phosphatase, receptor type, N precursor; islet cell antigen 2; islet cell antigen 512; islet cell autoantigen 3; protein tyrosine phosphatase-like N precursor	1389	0

				Q16849	PTPN_HUMAN Protein-tyrosine phosphatase-like N precursor (R-PTP-N) (PTP IA-2)(Islet cell antigen 512) (ICA 512) (Islet cell autoantigen 3)	1389	0
				AAA90974.1	tyrosine phosphatase	1389	0
				CAA44688.2	Islet Cell Antigen 512	972	0
				AAH07713.1	AAH07713 protein tyrosine phosphatase, receptor type, N	972	0
				I37577	islet cell antigen 512	850	0
					protein tyrosine phosphatase, receptor type, N polypeptide 2, isoform 2 precursor; protein tyrosine phosphatase receptor pi; phogrin; tyrosine phosphatase IA-2 beta; IAR/receptor-like protein-tyrosine phosphatase	607	e-173
				NP_570857.1		607	e-173
				AAB68603.1	protein tyrosine phosphatase receptor pi	607	e-173
					protein tyrosine phosphatase, receptor type, N polypeptide 2, isoform 1 precursor; protein tyrosine phosphatase receptor pi; phogrin; tyrosine phosphatase IA-2 beta; IAR/receptor-like protein-tyrosine phosphatase	607	e-173
				NP_002838.1		607	e-173
				Q92932	PTPX_HUMAN Protein-tyrosine phosphatase X precursor (R-PTP-X) (Islet cell autoantigen related protein) (ICAAR) (IAR) (Phogrin)	607	e-173
				JC5062	phogrin precursor	607	e-173
				AAC50742.1	phogri	607	e-173
				JC5263	transmembrane tyrosine phosphatase-like protein, ICAAR	607	e-173
				CAA69880.	Islet Cell Autoantigen Related	607	e-173
				AAB63600.1	IAR/receptor-like protein-tyrosine phosphatase precursor	607	e-173
				BAA20841.2	KIAA0387	607	e-173
					protein tyrosine phosphatase, receptor type, N polypeptide 2, isoform 3 precursor; protein tyrosine phosphatase receptor pi; phogrin; tyrosine phosphatase IA-2 beta; IAR/receptor-like protein-tyrosine phosphatase	579	e-164
				NP_570858.1		579	e-164
				AAH34040.1	protein tyrosine phosphatase, receptor type, N polypeptide 2	481	e-152
				AAK74066.1	odd-skipped-related 2A protein		
NM_054049		U:(C-IR) 2.03					
NP_473390.1	Mm.4633 6	U:(C-IR) 2.46					
				BAC11035.1	unnamed protein product	484	e-152
				AAH16936.1	AAH16936 odd-skipped-related 2A protein	509	e-144

				NP_443727.1	odd-skipped-related 2A protein	507	e-143
				AAK74067.1	odd-skipped-related 2B protein	507	e-143
				XP_059439.2	similar to odd-skipped related 1 (Drosophila); odd-skipped related gene; odz (odd Oz/ten-m) homolog (Drosophila) related 1	347	2e-95
				NP_660303.1	similar to odd-skipped related 1 (Drosophila); odd-skipped related gene; odz (odd Oz/ten-m) homolog (Drosophila) related 1	347	2e-95
				AAH25712.1	Similar to odd-skipped related 1 (Drosophila)	347	2e-95
				BAB92079.1	zinc finger transcription factor	347	2e-95
				BAC11079.1	unnamed protein product	347	2e-95
NM_007924							
NP_031950.1	Mm.1552	U:(C-IR) 2.03		NP_006523.1	ELL gene (11-19 lysine-rich leukemia gene)	880	0
				P55199	ELL_HUMAN RNA polymerase II elongation factor ELL (Eleven-nineteen lysine-rich leukemia protein)	880	0
				I38880	eleven-nineteen lysine-rich leukemia gene (ELL) protein	880	0
				AAA57120.1	ELL	880	0
				AAB34056.1	MEN chimeric transcription factor	803	0
				NP_036213.1	ELL-related RNA polymerase II, elongation factor	371	e-102
				O00472	ELL2 HUMAN RNA polymerase II elongation factor ELL2	371	e-102
				AAC51232.1	RNA polymerase II elongation factor ELL2	371	e-102
				AAH28412.1	ELL-RELATED RNA POLYMERASE II, ELONGATION FACTOR	371	e-102
NM_008521							
NP_032547.1	Mm.4088	U:(C-IR) 2.03		AAH29498.1	leukotriene C4 synthase	204	5e-53
				JC5398	leukotriene C4 synthase (EC 6.-.-.-)	204	7e-53
				NP_665874.1	leukotriene C4 synthase isoform 1	204	7e-53
				Q16873	LC4S_HUMAN Leukotriene C4 synthase (Leukotriene-C(4) synthase) (LTC4 synthase)	204	7e-53
				I38595	leukotriene-C4-synthase (EC 2.5.1.37)	204	7e-53
				AAA20467.1	leukotriene C4 synthase	204	7e-53

				AAA50555.1	leukotriene-C4 synthase	204	7e-53
				AAC50476.1	leukotriene C4 synthase	204	7e-53
				AAB06723.1	leukotriene C4 synthase	204	7e-53
NM_010780 NP_034910.1	Mm.1252	U:(C-IR) 2.03		NP_001827.1	chymase 1, mast cell preproprotein; chymase, mast cell; chymase, heart; mast cell protease I	345	9e-95
				P23946	MCT1_HUMAN Chymase precursor (Mast cell protease I)	345	9e-95
				KYHUCM	chymase (EC 3.4.21.39) precursor [validated]	345	9e-95
				AAA52019.1	chymase	345	9e-95
				AAA52020.1	mast cell chymase	345	9e-95
				AAA52021.1	chymase	345	9e-95
				1KLT	Crystal Structure Of Pmsf-Treated Human Chymase At 1.9 Angstroms Resolution	333	2e-91
				AAB26828.1	chymase	333	2e-91
				1914144A	chymase	333	2e-91
				1PJP	A Chain A, The 2.2 A Crystal Structure Of Human Chymase In Complex With Succinyl-Ala-Ala-Pro-Phe-Chloromethylketone	331	1e-90
NM_021470 NP_067445.1	Mm.8735 2	U:(C-IR) 2.03		NP_112198.1	ring finger protein 32	522	e-148
				CAB66808.1	hypothetical protein	522	e-148
				AAG50281.1	AF325690_1 FKSG33	522	e-148
				AAM18664.1	AF441222_1 ring finger protein RNF32	522	e-148
				AAD43189.1	AC005534_2 supported by human ESTs AA412402 (NID:g2070990) NH44021 (NID:g1182549), mouse EST AA065933 (NID:g1562789), and genscan	445	e-125
				AAH15416.1	AAH15416 Similar to hypothetical protein DKFZp434C135	319	4e-87
				AAH28120.1	Similar to ring finger protein 32	310	2e-84
NM_007513 NP_031539.1	Mm.5255	U:(C-IR) 2.02		NP_003036.1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1; ecotropic retroviral receptor; Solute carrier family 7 (cationic amino acid transporter, y+ system); amino acid transporter, cationic 1	990	0
				P30825	CTR1_HUMAN High-affinity cationic amino acid transporter-1 (CAT-1) (CAT1) (System Y+ basic amino acid transporter) (Ecotropic retroviral leukemia receptor homolog) (ERR) (Ecotropic retrovirus receptor homolog)	990	0

			CAA41869.1	retroviral receptor		990	0
			AAC27721.1	cationic amino acid transporter		990	0
			S29685	retroviral receptor		988	0
			CAA40560.1	RECIL		988	0
			P52569	CTR2_HUMAN Low-affinity cationic amino acid transporter-2 (CAT-2) (CAT2)		654	0
			BAA06271.1	cationic amino acid transporter 2		654	0
				solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 2; Solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system);, amino acid transporter, cationic 2			
			NP_003037.1			648	0
			AAB62810.1	hCAT-2A		648	0
			NP_116192.2	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 3		640	0
			AAL37184.1	cationic amino acid transporter		640	0
			BAC11353.1	unnamed protein product		640	0
			AAH33816.1	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 3		639	0
			BAC11253.1	unnamed protein product		637	0
			BAB55118.1	unnamed protein product		421	e-117
			XP_036892.1	similar to Cationic amino acid transporter-4 (CAT-4) (CAT4)		411	e-114
			AAH08814.1	Unknown (protein for MGC:10733)		411	e-114
			NP_004164.1	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 4		393	e-109
			O43246	CTR4_HUMAN Cationic amino acid transporter-4 (CAT-4) (CAT4)		393	e-109
			CAA04263.1	cationic amino acid transporter 3		393	e-109
NM_007962							
NP_031988.1	Mm.33240	U:(C-IR) 2.02	NP_005788.1	epithelial V-like antigen 1 precursor		330	3e-90
			NP_658911.1	epithelial V-like antigen 1 precursor		330	3e-90
			O60487	EVA1_HUMAN Epithelial V-like antigen 1 precursor		330	3e-90
			AAC39762.1	epithelial V-like antigen precursor		330	3e-90
			AAF87240.1	AF275945_1 epithelial V-like antigen 1		330	3e-90
			AAG23183.1	AF304447_1 epithelial V-like antigen 1		330	3e-90

				AAH1774.1	epithelial V-like antigen 1		330	3e-90
NM_010393	Mm.1960	U:(C-IR)	P30461		IB05_HUMAN HLA class I histocompatibility antigen, B-13 B*1301 alpha chain precursor (B13.1)		420	e-117
NP_034523.1	32	2.02	I54442		MHC class I histocompatibility antigen HLA-B13 precursor		420	e-117
			AAA52657.1		MHC HLA-B13 precursor		420	e-117
			AAA59660.1		MHC HLA-B13 chain		420	e-117
			BAA08822.1		HLA-B*1302 antigen		420	e-117
			CAC17136.1		MHC class I antigen		420	e-117
			CAC17137.1		MHC class I antigen		418	e-117
			A45850		MHC class I histocompatibility antigen HLA-B13.1		418	e-117
			AAA59627.1		HLA-B13 protein		418	e-117
			BAA08821.1		HLA-B*1301 antigen		418	e-117
			AAA59618.1		glycosylation aa 86, alpha domain 1 aa 1-24, alpha domain 2 aa 25-114, alpha domain 3 aa 207-298		418	e-117
			CAC29063.1		MHC class I antigen		418	e-117
			AAA73509.1		MHC class I lymphocyte antigen		416	e-116
			AAD00010.1		HLA-B38		416	e-116
			AAB06829.1		MHC antigen		415	e-116
			AAA98506.1		MHC class I antigen HLA-B precursor		414	e-116
			I84488		lymphocyte antigen		413	e-115
			AAC31793.1		HLA class I antigen HLA-B		412	e-115
			P30476		IB32_HUMAN HLA class I histocompatibility antigen, B-39 B*3902 alpha chain precursor (B39.2)		412	e-115
			I68850		MHC class I histocompatibility antigen precursor		412	e-115
			AAA52659.1		lymphocyte antigen		412	e-115
			AAA87396.1		MHC class I antigen		412	e-115
X99104	Mm.1976	U:(C-IR)	NP_084656.1		GLI-Kruppel family member GLI2 isoform beta; oncogene GLI2; tax helper protein 2; zinc finger protein GLI2; tax-responsive element-25-bp sequence binding protein; tax-responsive element-2 holding protein		1821	0
	95	2.02						



				BAA25666.1	hGLI2		1821	0
				NP_084655.1	GLI-Kruppel family member GLI2 isoform alpha; oncogene GLI2; tax helper protein 2; zinc finger protein GLI2; tax-responsive element-25-bp sequence binding protein; tax-responsive element-2 holding protein		1810	0
				P10070	GLI2_HUMAN Zinc finger protein GLI2 (Tax helper protein)		1810	0
				BAA25665.1	hGLI2		1810	0
				NP_005261.1	GLI-Kruppel family member GLI2 isoform delta; oncogene GLI2; tax helper protein 2; zinc finger protein GLI2; tax-responsive element-25-bp sequence binding protein; tax-responsive element-2 holding protein		1263	0
				BAA25668.1	hGLI2		1263	0
				NP_084657.1	GLI-Kruppel family member GLI2 isoform gamma; oncogene GLI2; tax helper protein 2; zinc finger protein GLI2; tax-responsive element-25-bp sequence binding protein; tax-responsive element-2 holding protein		1252	0
				BAA25667.1	hGLI2		1252	0
				NP_000159.2	GLI-Kruppel family member GLI3; oncogene GLI3; DNA-binding protein; zinc finger protein GLI3		1043	0
				CAB59315.1	GLI3 protein		1043	0
				P10071	GLI3_HUMAN Zinc finger protein GLI3		1004	0
				A35927	190K DNA-binding protein GLI3		1004	0
				AAA52564.1	DNA-binding protein		1004	0
				BAA03568.1	Tax helper protein 1		730	0
				BAA03569.1	Tax helper protein 2		719	0
				NP_005260.1	glioma-associated oncogene homolog		445	e-124
				P08151	GLI1_HUMAN Zinc finger protein GLI1 (Glioma-associated oncogene) (Oncogene GLI)		445	e-124
				TVHUGL	transforming protein gli		445	e-124
				CAA30297.1	GLI protein (AA 1-1106)		445	e-124
				AAH13000.1	AAH13000 Similar to glioma-associated oncogene homolog (zinc finger protein)		445	e-124
				AAM13391.1	GLI1		445	e-124

NM_018790 NP_061260.1	Mm.2540 5	U:(C-IR) 2.01 U:(C-D) 2.34	BAA19667.1	Similar to Rat growth factor Arc (U19866)	765	0
			NP_056008.1	activity-regulated cytoskeleton-associated protein	763	0
			AAF07185.1	AF193421_1 ARC	763	0
			AAG33705.1	AF248637_1 activity-regulated cytoskeleton-associated protein	763	0
			AAH12321.1	AAH12321 Similar to activity-regulated cytoskeleton-associated protein	763	0
			NP_066013.1	DDM36	2055	0
NM_020043 NP_064427.1	Mm.1437 41	U:(C-IR) 2.01 U:(C-D) 2.17	BAB86306.1	hDDM36	2055	0
			BAB13454.1	KIAA1628 protein	1539	0
			AAC51287.1	neogenin	260	2e-68
			NP_002490.1	neogenin homolog 1 (chicken); neogenin (chicken) homolog 1	260	2e-68
			Q92859	NEO1_HUMAN Neogenin precursor	260	2e-68
			AAB17263.1	neogenin	260	2e-68
			NP_005206.1	deleted in colorectal carcinoma	226	2e-58
			P43146	DCC_HUMAN Tumor suppressor protein DCC precursor (Colorectal cancer suppressor)	226	2e-58
			A54100	tumor suppressor protein DCC precursor	226	2e-58
			CAA53735.1	tumour suppressor	226	2e-58
			AAA35751.1	colorectal tumor suppressor (put.); putative	216	3e-55
NM_013906 NP_038934.1	Mm.1005 82	U:(C-IR) 2.01 U:(C-D) 2.16	Q9UP79	ATS8_HUMAN ADAMTS-8 precursor (A disintegrin and metalloproteinase with thrombospondin motifs 8) (ADAM-TS8) (METH-2) (METH-8)	1404	0
			AAD48081.1	AF060153_1 METH2 protein	1404	0
			NP_008968.2	a disintegrin and metalloprotease with thrombospondin motifs-8	1403	0

				NP_008919.2	a disintegrin and metalloprotease with thrombospondin motifs-1 preproprotein; human metalloprotease with thrombospondin type 1 motifs	799	0
				AAF23772.1	AF207664_1 matrix metalloprotease	799	0
				BAA95502.1	metalloprotease with thrombospondin type 1 motifs	799	0
				AAD48080.1	AF060152_1 METH1 protein	798	0
				Q9UHI8	ATS1_HUMAN ADAMTS-1 precursor (A disintegrin and metalloprotease with thrombospondin motifs 1) (ADAM-TS1) (ADAM-TS1) (METH-1)	798	0
				AAF15317.1	AF170084_1 metalloprotease with thrombospondin type 1 motifs ADAMTS1	798	0
				BAA92584.1	KIAA1346 protein	798	0
				AAH36515.1	Unknown (protein for MGC:32979)	795	0
				NP_620686.1	a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 15 preproprotein	733	0
				CAC86014.1	metalloprotease disintegrin 15 with thrombospondin domains	733	0
NM_013866 NP_038894.1	Mm.1409 9	U:(C-IR) 2.01		XP_028643.4	similar to DKFZP586G1122 protein	543	e-154
				NP_056296.1	DKFZP586G1122 protein	543	e-154
				AAL08625.1	AF304052_1 hematopoietic zinc finger protein	543	e-154
				AAH29752.1	DKFZP586G1122 protein	543	e-154
				T17248	hypothetical protein DKFZp586G1122.1	426	e-119
				CAB55938.1	hypothetical protein	426	e-119
				BAB14910.1	unnamed protein product	321	3e-87
				NP_078973.1	hypothetical protein FLJ22419	279	1e-74
				BAB15350.1	unnamed protein product	279	1e-74
				AAH07212.1	AAH07212 hypothetical protein FLJ22419	279	1e-74
				BAC04870.1	unnamed protein product	266	1e-70
				NP_689733.1	hypothetical protein FLJ25270	263	1e-69
				BAB71629.1	unnamed protein product	263	1e-69
				XP_087103.1	similar to zinc finger protein 385; hematopoietic zinc finger	262	1e-69
				AAH38422.1	hypothetical protein FLJ25270	262	1e-69

NM_019762 NP_062736.1	Mm.2960 3	U:(C-IR) 2.01	NP_009114.1	plakophilin 3	1271	0
			Q9Y446	PKP3_HUMAN Plakophilin 3	1271	0
			CAB44310.1	plakophilin 3	1271	0
			AAF23050.1	AF053719_1 plakophilin-3 protein	1271	0
			AAH00081.1	AAH00081 plakophilin 3	1271	0
			CAA66265.1	plakophilin 2a	243	9e-64
			AAB97957.1	arm-repeat protein NPRAP/neurojungin	237	6e-62
			AAD00453.1	GT24	237	8e-62
			NP_001323.1	catenin (cadherin-associated protein), delta 2 (neural plakophilin-related arm-repeat protein); catenin (cadherin-associated protein), delta 2	237	8e-62
			BAA36163.1	neural plakophilin-related arm-repeat protein (NPRAP)	237	8e-62
			Q9UQB3	CTD2_HUMAN Catenin delta-2 (Delta-catenin) (Neural plakophilin-related ARM-repeat protein) (NPRAP) (Neurojungin) (GT24)	232	3e-60
			AAC63103.1	delta-catenin	232	3e-60
			S60712	band-6-protein	228	4e-59
			CAA55881.1	band-6-protein	228	4e-59
			NP_000290.1	plakophilin 1; Plakophilin-1	225	2e-58
			CAA84426.1	plakophilin	225	2e-58
			CAA98022.1	plakophilin 1	225	2e-58
			NP_004563.1	plakophilin 2	222	2e-57
			Q99959	PKP2_HUMAN Plakophilin 2	222	2e-57
			CAA66264.1	plakophilin 2b	222	2e-57
			NP_003619.1	plakophilin 4	222	3e-57
			Q99569	PKP4_HUMAN Plakophilin 4	222	3e-57
			CAA57478.1	p0071 protein	222	3e-57
NM_028089 NP_082365.1	Mm.1425 81	U:(C-IR) 2	NP_000763.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 18; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 17; microsomal monooxygenase; flavoprotein-linked monooxygenase	766	0

			AAB59356.1	cytochrome		766	0
			P33260	CPCI_HUMAN Cytochrome P450 2C18 (CYPIIC18) (P450-6B/29C)		764	0
			A61269	cytochrome P450 2C18		764	0
			AAA02630.1	cytochrome P-4502C18		764	0
			AAB23864.2	cytochrome P-450		736	0
			NP_000762.2	cytochrome P450, subfamily IIC, polypeptide 9; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 10; mephenytoin 4-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase		736	0
			P11712	CPC9_HUMAN Cytochrome P450 2C9 (CYPIIC9) (P450 PB-1) (P450 MP-4) (S-mephenytoin 4-hydroxylase) (P-450MP)		736	0
			B38462	S-mephenytoin 4-hydroxylase (EC 1.14.14.-) cytochrome P450 2C9		736	0
			I313295A	cytochrome P450		736	0
			BAA00123.1	cytochrome P-450		736	0
			P11713	CPCA_HUMAN Cytochrome P450 2C10 (CYPIIC10) (P450 MP-8) (S-mephenytoin 4-hydroxylase) (P-450MP)		729	0
			D28951	cytochrome P450 2C10		729	0
			AAAS2157.1	cytochrome P-450 S-mephenytoin 4-hydroxylase		729	0
			AAAS2158.1	cytochrome P-450 S-mephenytoin 4-hydroxylase		729	0
			I506290A	cytochrome P450		728	0
			NP_000760.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 19; mephenytoin 4'-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase		726	0
			P33261	CPCJ_HUMAN Cytochrome P450 2C19 (CYPIIC19) (P450-11A) (Mephenytoin 4-hydroxylase) (CYPIIC17) (P450-254C)		726	0
			AAB59426.1	cytochrome		726	0
			F38462	S-mephenytoin 4'-hydroxylase (EC 1.14.14.-) cytochrome P450 2C19		722	0
NM_010689	Mm.1028	U:(C-IR) 13.11	CAA11218.1	36 kDa phosphotyrosine protein		231	2e-60
NP_034819.1	10	U:(C-D) 2.17					

			AAC39636.1	LAT		231	2e-60
			AAH11563.1	AAH11563 Similar to linker for activation of T cells		231	2e-60
			NP_055202.1	linker for activation of T cells		215	1e-55
			O43561	LAT_HUMAN Linker for activation of T cells (36 kDa phospho-tyrosine adaptor protein) (pp36) (p36-38)		215	1e-55
			AAC39637.1	LAT		215	1e-55
NM_017370	Mm.2673	U:(C-D)	CAA25926.1	haptoglobin		599	e-171
NP_059066.1	0	6.81	P00737	HPT1_HUMAN Haptoglobin-1 precursor		598	e-171
			HPHU1	haptoglobin precursor, allele 1 [validated]		598	e-171
			AAA52684.1	preprohaptoglobin		598	e-171
			CAA25267.1	haptoglobin alpha 1S		598	e-171
			AAC27432.1	haptoglobin		597	e-170
			NP_066275.2	haptoglobin-related protein; Haptoglobin-related locus		569	e-162
			P00739	HPTR_HUMAN Haptoglobin-related protein precursor		569	e-162
			HPHUR	haptoglobin-related protein precursor		569	e-162
			AAA88079.1	haptoglobin-related protein		569	e-162
			AAA88081.1	haptoglobin-related protein		569	e-162
			CAA25927.1	haptoglobin		568	e-162
			AAC27433.1	haptoglobin-related protein precursor		565	e-161
			CAA61501.1	haptoglobin-related protein		565	e-161
			AAA52687.1	haptoglobin precursor		559	e-159
			NP_005134.1	haptoglobin		559	e-159
			P00738	HPT2_HUMAN Haptoglobin-2 precursor		559	e-159
			HPHU2	haptoglobin precursor, allele 2		559	e-159
			CAA25137.1	haptoglobin precursor		559	e-159
			AAA88078.1	haptoglobin		559	e-159
			AAA88080.1	haptoglobin		559	e-159

				AAA52685.1	preprohaptoglobin		559	e-159
				1006264A	haptoglobin Hp2		508	e-144
NM_007424		U:(C-D) 4.11			aggrecan 1 isoform 2 precursor; Aggrecan-1 (chondroitin sulfate proteoglycan-1, large aggregating proteoglycan, antigen identified by monoclonal antibody A0122);			
NP_031450.1	Mm.2759	U:(IR-D) 3.08		NP_037359.1	chondroitin sulfate proteoglycan 1, large aggregating proteoglycan	1795	0	
					aggrecan 1 isoform 1 precursor; Aggrecan-1 (chondroitin sulfate proteoglycan-1, large aggregating proteoglycan, antigen identified by monoclonal antibody A0122);			
				NP_001126.1	chondroitin sulfate proteoglycan 1, large aggregating proteoglycan	1794	0	
				AAA62824.1	large aggregating cartilage proteoglycan core protein	1794	0	
				A39086	aggrecan precursor, cartilage long splice form	1792	0	
					Similar to aggrecan 1 (chondroitin sulfate proteoglycan 1, large aggregating proteoglycan, antigen identified by monoclonal antibody A0122)	1253	0	
				AAH36445.1	cartilage specific proteoglycan (600 AA)	823	0	
				CAA35463.1	proteoglycan core protein	573	e-162	
				AAA35726.1	chondroitin sulfate proteoglycan BEHAB/brevican	369	e-101	
				AAH10571.1	AF228710_1 chondroitin sulfate proteoglycan BEHAB/brevican	369	e-101	
				AAG23134.1	AF229053_1 chondroitin sulfate proteoglycan BEHAB/brevican	369	e-101	
				AAG23135.1	ras-related C3 botulinum toxin substrate 2; Ras-related C3 botulinum toxin substrate 3 (rho family, small GTP-binding protein Rac2); rho family, small GTP binding protein Rac2	390	e-108	
NM_009008		U:(C-D) 2.85			RAC2_HUMAN Ras-related C3 botulinum toxin substrate 2 (p21-Rac2) (Small G protein) (GX)	390	e-108	
NP_033034.1	Mm.1972			NP_002863.1	GTP-binding protein rac2	390	e-108	
				P15153	A Chain A, Crystal Structure Of A Rac-Rhogdi Complex	390	e-108	
				B34386	ras-related C3 botulinum toxin substrate	390	e-108	
				IDS6	rac1 p21=small GTP-binding protein [human, HL60, Peptide, 192 aa]	390	e-108	
				AAA36538.1	dJ151B14.2' (ras-related C3 botulinum toxin substrate 2 (rho family, mall GTP binding protein Rac2))	390	e-108	
				AAAB22207.1	AAH01485 ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	390	e-108	
				CAB45265.1		390	e-108	
				AAH01485.1		390	e-108	

			AAM21112.1	AF498965_1 small GTP binding protein RAC2	390	e-108
			NP_008839.2	ras-related C3 botulinum toxin substrate 1 isoform Rac1; rho family, small GTP binding protein Rac1	367	e-101
			P15154	RAC1_HUMAN Ras-related C3 botulinum toxin substrate 1 (p21-Rac1) (Ras-like protein TC25)	367	e-101
			TVHUC1	GTP-binding protein rac1	367	e-101
			I14D	D Chain D, Crystal Structure Analysis Of Rac1-Gdp Complexed With Arfaptin (P21)	367	e-101
			I14L	D Chain D, Crystal Structure Analysis Of Rac1-Gdp In Complex With Arfaptin (P41)	367	e-101
			AA336537.1	ras-related C3 botulinum toxin substrate	367	e-101
			AAB22206.1	rac1 p21=small GTP-binding protein [human, HL60, Peptide, 192 aa]	367	e-101
			CAB53579.5	Rac1 protein	367	e-101
			AAM21111.1	AF498964_1 small GTP binding protein RAC1	367	e-101
			AAH04247.1	AAH04247 ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)	367	e-101
			AAA35941.1	small G protein	366	e-101
			AAA36544.1	ras-like protein	366	e-101
			I14T	D Chain D, Crystal Structure Analysis Of Rac1-Gmppnp In Complex With Arfaptin	365	e-100
			1e+96	A Chain A, Structure Of The RacP67PHOX COMPLEX	363	e-100
			1HH4	A Chain A, Rac1-Rhogdi Complex Involved In NADPH Oxidase Activation	362	e-100
			1HH4	B Chain B, Rac1-Rhogdi Complex Involved In NADPH Oxidase Activation	362	e-100
			NP_005043.1	ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3); rho family, small GTP binding protein Rac3		
			O14658	RAC3_HUMAN Ras-related C3 botulinum toxin substrate 3 (p21-Rac3)	358	1e-98
			AAC51667.1	Rac3	358	1e-98
			AAH15197.1	AAH15197 ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3)	358	1e-98
			AAH09605.1	AAH09605 ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3)	358	1e-98
			AAM21113.1	AF498966_1 small GTP binding protein RAC3	358	1e-98



				NP_061485.1	ras-related C3 botulinum toxin substrate 1 isoform Rac1b; rho family, small GTP binding protein Rac1	356	5e-98
				CAA10732.1	small GTPase rac1b	356	5e-98
				AAD30547.1	AF136373_1 ras-related C3 botulinum toxin substrate isoform	356	5e-98
				CAA10733.6	Rac1b protein	356	5e-98
AK013740							
BAB28979.1	Mm.27579	U:(C-D) 2.82		NP_068747.1	hypothetical protein FLJ22649 similar to signal peptidase SPC22/23	298	1e-80
				BAB15437.1	unnamed protein product	298	1e-80
				Q9H0S7	SP22_HUMAN Microsomal signal peptidase 23 kDa subunit (SPase 22 kDa subunit)	295	9e-80
				CAB66595.1	hypothetical protein	295	9e-80
X00496		U:(C-D) 2.81		NP_004346.1	CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated); CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)	226	4e-59
CAA25191.1	Mm.7043						
				CAA25192.1	putative p33	226	4e-59
				AAA36033.1	cell surface glycoprotein	226	4e-59
				AAH18726.1	AAH18726 CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)	226	4e-59
				HLHUG	class II histocompatibility antigen-associated gamma chain	226	4e-59
				CAA25193.1	putative p33	226	4e-59
				AAA36304.1	class II antigen gamma chain	226	4e-59
				CAA27047.1	gamma chain	225	9e-59
				P04233	HG2A_HUMAN HLA class II histocompatibility antigen, gamma chain (HLA-DR antigens associated invariant chain) (Ia antigen-associated invariant chain) (ii) (p33) (CD74 antigen)	207	1e-53
NM_015737	Mm.5699	U:(C-D) 2.72					
NP_056552.1	1	U:(IR-D) 2.1		AAH36390.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 4 (GalNAc-T4)	1078	0

			NP_003765.1	polypeptide N-acetylglucosaminyltransferase 4; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylglucosaminyltransferase 4; GalNAc transferase 4; UDP-GalNAc: polypeptide N-acetylglucosaminyltransferase 4; protein-UDP acetylglucosaminyltransferase 4	1073	0
			CAA69875.1	UDP-GalNAc:polypeptide N-acetylglucosaminyltransferase	1073	0
			CAC80100.2	UDP-GalNAc-transferase 12	624	e-178
			NP_078918.2	hypothetical protein FLJ21212; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylglucosaminyltransferase 12(GalNAc-T12)	622	e-178
			BAC07181.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylglucosaminyltransferase 12	622	e-178
			NP_004473.1	polypeptide N-acetylglucosaminyltransferase 3; protein-UDP acetylglucosaminyltransferase	462	e-130
			CAA63371.1	UDP-GalNAc:polypeptide N-acetylglucosaminyltransferase (GalNAc-T3)	462	e-130
			AAH35822.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylglucosaminyltransferase 6 (GalNAc-T6)	461	e-129
			BAC11118.1	unnamed protein product	461	e-129
			NP_009141.1	polypeptide N-acetylglucosaminyltransferase 6; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylglucosaminyltransferase 6; UDP-GalNAc:polypeptide N-acetylglucosaminyltransferase 6; protein-UDP acetylglucosaminyltransferase 6; GalNAc transferase 6	459	e-129
			CAA69876.1	UDP-GalNAc:polypeptide N-acetylglucosaminyltransferase	459	e-129
			BAB67811.1	KIAA1918 protein	417	e-116
			NP_065207.2	polypeptide N-acetylglucosaminyltransferase 1; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylglucosaminyltransferase 1; GalNAc-T1; GalNAc transferase 1; protein-UDP acetylglucosaminyltransferase 1; UDP-GalNAc:polypeptide N-acetylglucosaminyltransferase 1	416	e-116
			Q10472	PAGT_HUMAN Polypeptide N-acetylglucosaminyltransferase (Protein-UDP acetylglucosaminyltransferase) (UDP-GalNAc:polypeptide, N-acetylglucosaminyltransferase) (GalNAc-T1)	416	e-116
			JC4223	polypeptide N-acetylglucosaminyltransferase (EC 2.4.1.41)	416	e-116
			CAA59380.1	UDP-GalNAc:polypeptide N-acetylglucosaminyl transferase	416	e-116

NM_018866 NP_061354.1	Mm.1011 6	U:(C-D) 2.65					
NM_008458							
NP_032484.1	Mm.14191	U:(C-D) 2.59	CAA48671.1	alpha1-antichymotrypsin		494	e-139
			XP_028322.1	similar to Alpha-1-antichymotrypsin precursor (ACT)		490	e-138
			P01011	AACT_HUMAN Alpha-1-antichymotrypsin precursor (ACT)		490	e-138
			AAH03559.1	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3		490	e-138
			AAH10530.1	Unknown (protein for MGC:18102)		490	e-138
			AAH34554.1	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3		489	e-138
			AAD08810.1	alpha-1-antichymotrypsin precursor		478	e-134
			ITHUC	alpha-1-antichymotrypsin precursor		476	e-134
			AAA51560.1	alpha-1-antichymotrypsin precursor		470	e-132
			1QMN	A Chain A, Alpha1-Antichymotrypsin Serpin In The Delta Conformation (Partial Loop Insertion)		460	e-129
			1313184C	chymotrypsin inhibitor		441	e-123
			NP_001076.1	alpha-1-antichymotrypsin, precursor; alpha-1-antichymotrypsin; antichymotrypsin		439	e-123
			AAA51543.1	alpha-1-antichymotrypsin		439	e-123
			2ACH	A Chain A, Alpha1 Antichymotrypsin		434	e-121
NM_010382 NP_034512.1	Mm.2256 4	U:(C-D) 2.59	AAH07920.1	AAH07920 Unknown (protein for MGC:14111)		390	e-108
			AAL40069.1	L76133_1 lymphocyte antigen		390	e-108
			AAH08403.1	AAH08403 Similar to major histocompatibility complex, class II, DR beta 5		387	e-107
			CAC08827.1	MHC class II antigen		386	e-107
			I54448	MHC class II histocompatibility antigen DR beta 1 chain precursor		386	e-107
			AAA59713.1	precursor		386	e-107

					CAC08823.1	MHC class II antigen		386	e-107
					P20039	HB2I_HUMAN HLA class II histocompatibility antigen, DR-5 beta chain precursor		385	e-107
					A25324	class II histocompatibility antigen HLA-DR-5 beta chain precursor		385	e-107
					AAA36274.1	MHC HLA DR5 cell surface glycoprotein beta chain precursor		385	e-107
					CAC08826.2	MHC class II antigen		385	e-107
					P13760	HB2H_HUMAN HLA class II histocompatibility antigen, DR-4 beta chain precursor (DRB1*0401)		385	e-107
					A29310	MHC class II histocompatibility antigen HLA-DR beta 1 chain DR4 precursor		385	e-107
					CAC19360.1	dJ863G3.2 (major histocompatibility complex, class II, DR beta 1)		385	e-107
					CAB75359.1	human leucocyte antigen DRB1		385	e-107
					P01912	HB2B_HUMAN HLA class II histocompatibility antigen, DR-1 beta chain precursor (Clone P2-beta-3)		385	e-107
						pir  HLHU3D MHC class II histocompatibility antigen HLA-DR beta 1 chain DR17 precursor		385	e-107
					CAA25295.1	precursor		385	e-107
					CAB06490.1	dJ93N13.3 (major histocompatibility complex, class II, DR beta 1 (clone P2-beta-3))		385	e-107
AK012581									
XP_126675.1				U:(C-D) Mm.21687	AAK67634.1	hypothetical protein SB143		240	2e-63
					NP_085053.1	hypothetical protein MGC10986		240	2e-63
					AAH04400.1	Unknown (protein for MGC:10986)		240	2e-63
					BAC03855.1	unnamed protein product		240	2e-63
NM_027209				U:(C-D) 2.47	NP_690591.1	membrane-spanning 4-domains, subfamily A, member 6A isoform 1; CD20-like precursor; membrane-spanning 4-domains, subfamily A, member 6; four-span transmembrane protein 3.2; MS4A6A-polymorph; four-span transmembrane protein 3.1; HAIRB-iso		233	5e-61
NP_081485.1				Mm.2948 7					
					AAG41780.1	AF212240_1 CDA01		233	5e-61
					AAK37417.1	AF237908_1 MS4A6A protein		233	5e-61

				AAK37994.1	AF286866_1 MS4A6A-polymorph		233	5e-61
				AAH22854.1	membrane-spanning 4-domains, subfamily A, member 6A		232	8e-61
				AAL56222.1	AF350502_1 four-span transmembrane protein 3.1		229	5e-60
				AAG44626.1	AF253977_1 HAIRB-iso		222	1e-57
				NP_071744.2	membrane-spanning 4-domains, subfamily A, member 6A isoform 2; CD20-like precursor; membrane-spanning 4-domains, subfamily A, member 6; four-span transmembrane protein 3.2; MS4A6A-polymorph; four-span transmembrane protein 3.1; HAIRB-iso		208	1e-53
				AAL07357.1	AF354930_1 MS4A6A		208	1e-53
				AAG27920.1	AF142409_1 CD20-like precursor		207	2e-53
				AAL56223.1	AF350503_1 four-span transmembrane protein 3.2		207	4e-53
NM_011116 NP_035246.1	Mm.6483	U:(C-D) 2.45		AAH36327.1	Similar to phospholipase D3		890	0
				AAH00553.1	AAH00553 similar to vaccinia virus HindIII K4L ORF		818	0
				NP_036400.1	similar to vaccinia virus HindIII K4L ORF		816	0
				AAB16799.1	HU-K4		816	0
				NP_620145.1	hypothetical protein BC015003		385	e-106
				AAH15003.1	AAH15003 Unknown (protein for MGC:23565)		385	e-106
				NP_689879.1	hypothetical protein FLJ40773		275	2e-73
				BAC05230.1	unnamed protein product		275	2e-73
				BAC03722.1	unnamed protein product		223	9e-58
NM_013487 NP_038515.1	Mm.4527	U:(C-D) 2.39		NP_000723.1	CD3D antigen, delta polypeptide (TtT3 complex)		228	5e-60
				P04234	CD3D_HUMAN T-cell surface glycoprotein CD3 delta chain precursor (T-cell receptor T3 delta chain)		228	5e-60
				RWHUD1	T-cell surface glycoprotein CD3 delta chain precursor		228	5e-60
				CAA25683.1	20K T3 glycoprotein precursor		228	5e-60
				AAA51792.1	T3 antigen delta-chain		228	5e-60
				CAA27573.1	T3 delta protein		228	5e-60

AK004773				1101394A	protein delta T3.glyco	222	2e-58
XP_125911.2	Mm.32580	U:(C-D) 2.27		NP_055686.1	KIAA0710 gene product	1150	0
				BAA31685.1	KIAA0710 protein	1150	0
				AAH24043.1	KIAA0710 gene product	1141	0
NM_007804							
NP_031830.1	Mm.5116	U:(C-D) 2.26		O14529	CUT2_HUMAN Homeobox protein Cux-2 (Cut-like 2)	1950	0
				BAA22962.2	The human homolog of mouse Cux-2	1950	0
				XP_027045.6	similar to Homeobox protein Cux-2 (Cut-like 2)	1949	0
				P39880	CUT1_HUMAN CCAAT displacement protein (CDP) (Cut-like 1)	892	0
				AAB26579.1	CCAAT displacement protein, CDP [human, Peptide, 1505 aa]	892	0
				NP_001904.1	cut-like 1, CCAAT displacement protein; cut like 1, CCAAT displacement protein (Drosophila)	283	2e-75
				AAA35654.1	alternatively spliced	283	2e-75
				AAH25422.1	cut-like 1, CCAAT displacement protein (Drosophila)	283	2e-75
				AAG59620.1	AF271236_1 transcription factor CUX2	238	8e-62
NM_026384	Mm.1801	U:(C-D) 2.26		CAD38961.1	hypothetical protein	761	0
NP_080660.1	89						
				NP_115953.2	diacylglycerol O-acyltransferase homolog 2; GS1999full	751	0
				AAH15234.1	AAH15234 Unknown (protein for MGC:17861)	751	0
				AAK84176.2	AF384161_1 diacylglycerol acyltransferase 2	751	0
				BAB40641.2	product is unknown	751	0
				CAD13492.1	bA351K23.5 (novel protein)	340	2e-93
				NP_477513.1	diacylglycerol O-acyltransferase 2 like 1; diacylglycerol acyltransferase 2-like	331	1e-90
				AAK84178.1	AF384163_1 diacylglycerol acyltransferase 2-like protein	331	1e-90
				AAD45832.1	AC004876_5 similar to predicted proteins AAB54240 (PID:g2088822) and S67138 (PID:g2132925)	295	1e-79

				XP_088691.1	similar to bA351K23.5 (novel protein)	251	1e-66
				XP_088683.1	similar to bA351K23.5 (novel protein)	219	5e-57
				XP_093119.2	similar to bA351K23.5 (novel protein)	215	1e-55
				NP_079374.1	hypothetical protein FLJ22644	206	5e-53
				BAB15436.1	unnamed protein product	206	5e-53
AK004809							
BAB23580.1	Mm.28152	U:(C-D) 2.25		AAN41656.1	ezrin-binding protein PACE-1	1081	0
				CAB55300.1	hypothetical protein	956	0
				CAB52564.2	dJ97P20.1 (novel gene)	956	0
				AAN23123.1	ezrin-binding partner PACE-1	956	0
				NP_065156.4	ezrin-binding partner PACE-1	954	0
				AAH14662.1	Similar to hypothetical protein LOC57147	954	0
NM_009151							
NP_033177.1	Mm.22173	U:(C-D) 2.25		XP_006867.4	similar to P-selectin glycoprotein ligand 1 precursor (PSGL-1) (Selectin P ligand) (CD162 antigen)	286	5e-77
				Q14242	SEPL_HUMAN P-selectin glycoprotein ligand 1 precursor (PSGL-1) (Selectin P ligand) (CD162 antigen)	286	5e-77
				A57468	P-selectin glycoprotein ligand PSGL-1 precursor, long splice form	286	5e-77
				AAA74577.1	P-selectin glycoprotein ligand	286	5e-77
				NP_002997.1	selectin P ligand	284	2e-76
				AAC50061.1	ligand for P-selectin	284	2e-76
				AAH29782.1	selectin P ligand	284	2e-76
				BAC05283.1	unnamed protein product	258	2e-68
NM_030255	Mm.8970	U:(C-D) 2.24		NP_660341.2	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F; similar to Phorbol 3 (APOBEC1-like)	200	7e-51
NP_084531.1	2			AAH38808.1	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F	199	1e-50
AK009960							
XP_133997.2	Mm.28248	U:(C-D) 2.23		BAA96067.1	KIAA1543 protein	388	e-108

			XP_048362.1	similar to KIAA1543 protein	388	e-108
			CAD38783.1	hypothetical protein	388	e-108
			AAL55764.1	AF289580_1 unknown	320	1e-87
			XP_036589.2	similar to KIAA1078 protein	237	2e-62
			AAH11385.1	Unknown (protein for IMAGE:3870900)	237	2e-62
			BAA83030.2	KIAA1078 protein	237	2e-62
			T14744	hypothetical protein DKFZp586F0424.1	236	3e-62
			CAB53664.1	hypothetical protein	236	3e-62
			AAH12778.1	Unknown (protein for IMAGE:3939659)	227	1e-59
			CAD39184.1	hypothetical protein	227	1e-59
NM_024249			NP_612637.1	hypothetical protein MGCI5523	689	0
NP_077211.2	Mm.3310	U:(C-D) 2.23				
			AAH14642.1	AAH14642 Similar to RIKEN cDNA 1810073N04 gene	689	0
			BAC04027.1	unnamed protein product	275	1e-73
NM_030562	Mm.1832	U:(C-D) 2.21	BAA96008.1	KIAA1484 protein	701	0
NP_085039.1	64					
			XP_046088.1	similar to hypothetical protein MGC7599; clone MGC:7599	670	0
			XP_085176.1	similar to hypothetical protein MGC2656	484	e-136
			NP_689660.1	hypothetical protein FLJ30803	484	e-136
			BAB70910.1	unnamed protein product	484	e-136
			BAA86560.1	KIAA1246 protein	466	e-131
			XP_166372.1	similar to hypothetical protein MGC2656	466	e-131
			NP_078785.1	hypothetical protein MGC2656	446	e-125
			AAH03578.1	AAH03578 Unknown (protein for MGC:2656)	446	e-125
			AAH25310.1	Similar to KIAA1484 protein	431	e-120
			NP_076941.2	hypothetical protein MGC3103	424	e-118
			AAH15581.2	similar to hypothetical protein MGC3103	424	e-118
			AAH14678.1	AAH14678 Unknown (protein for IMAGE:3860672)	274	2e-73



NM_033614 NP_291092.1	Mm.1969 71	U:(C-D) 2.15	JC4520	3',5'-cyclic-GMP phosphodiesterase (EC 3.1.4.35) alpha' chain	1489	0
			CAA64079.1	cone cGMP phosphodiesterase	1489	0
			2207224A	cGMP phosphodiesterase	1489	0
			P51160	CNRC_HUMAN Cone cGMP-specific 3',5'-cyclic phosphodiesterase alpha'-subunit	1484	0
			AA92886.1	cone photoreceptor cGMP-phosphodiesterase alpha' subunit	1484	0
			NP_006195.2	phosphodiesterase 6C, cGMP-specific, cone, alpha prime	1478	0
			AA96392.1	phosphodiesterase A' subunit	1478	0
			NP_000274.1	phosphodiesterase 6B, cGMP-specific, rod, beta	1092	0
			P35913	CNRB_HUMAN Rod cGMP-specific 3',5'-cyclic phosphodiesterase beta-subunit (GMP-PDE beta)	1092	0
			A42828	3',5'-cyclic-GMP phosphodiesterase (EC 3.1.4.35) beta chain	1092	0
			AAB22690.1	rod cGMP phosphodiesterase beta-subunit; PDEB	1092	0
			CAA46932.1	3',5'-cyclic-nucleotide phosphodiesterase	1092	0
			AAH00249.1	AAH00249 phosphodiesterase 6B, cGMP-specific, rod, beta (congenital stationary night blindness 3, autosomal dominant)	1089	0
			CAA44569.1	cGMP phosphodiesterase beta subunit	1085	0
			B34611	3',5'-cyclic-GMP phosphodiesterase (EC 3.1.4.35) alpha chain	1075	0
			NP_000431.1	phosphodiesterase 6A, alpha subunit	1074	0
			P16499	CNRA_HUMAN Rod cGMP-specific 3',5'-cyclic phosphodiesterase alpha-subunit (GMP-PDE alpha) (PDE V-B1)	1074	0
			AAB69155.1	cGMP phosphodiesterase	1074	0
			CAA62215.1	Rod cGMP phosphodiesterase	893	0
			NP_058649.2	phosphodiesterase 11A; cyclic nucleotide phosphodiesterase 11A1	409	e-113
			BAB16371.1	phosphodiesterase 11A	409	e-113
			BAB62712.1	phosphodiesterase 11A4	409	e-113
NM_007441						
NP_031467.1	Mm.10112	U:(C-D) 2.14	NP_006483.1	aristal-less-like homeobox 3	516	e-146

				O95076	ALX3_HUMAN Homeobox protein aristaless-like 3 (Proline-rich transcription factor ALX3)	516	e-146
				AAD01418.1	homeobox protein	516	e-146
NM_017394 NP_059090.1	Mm.3556 7	U:(C-D) 2.14		NP_062823.1	solute carrier family 7, member 10; asc-type amino acid transporter 1	904	0
				Q9NS82	AAA1_HUMAN Asc-type amino acid transporter 1 (Asc-1)	904	0
				BAB03213.1	asc-type amino acid transporter 1	904	0
				AAK93960.1	AF340165_1 amino acid transporter	904	0
				CAC81900.1	ASC1 protein	904	0
				AAH35627.1	similar to solute carrier family 7	904	0
				Q9UHI5	LAT2_HUMAN Large neutral amino acids transporter small subunit 2 (L-type amino acid transporter 2) (hLAT2)	669	0
				AAF20381.1	AF171669_1 glycoprotein-associated amino acid transporter LAT2	669	0
				BAB21519.1	L-type amino acid transporter 2	669	0
				NP_036376.1	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 8	666	0
				CAB40137.1	SLC7A8 protein	666	0
				AAF05695.1	AF135828_1 L amino acid transporter-2; LAT-2	534	e-151
				NP_003477.2	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 5; Membrane protein E16; Solute carrier family 7, member 5; 4F2 light chain	436	e-122
				Q01650	LAT1_HUMAN Large-neutral amino acids transporter small subunit 1 (L-type amino acid transporter 1) (4F2 light chain) (4F2 LC) (4F2LC) (CD98 light chain) (Integral membrane protein E16) (hLAT1)	436	e-122
				JG0165	LAT1 protein	436	e-122
				BAA33851.1	CD98 light chain	436	e-122
				AAD20464.1	L-type amino acid transporter subunit LAT1	436	e-122
				BAA84648.1	L-type amino acid transporter 1	436	e-122
				AAC61479.1	amino acid transporter E16	436	e-122
				AAH39692.1	Similar to solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 5	436	e-122

				BAA75746.1	4F2 light chain		434	e-121
				BAB70708.1	sodium-independent neutral amino acid transporter LAT1		434	e-121
				NP_003974.1	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 6		431	e-120
				BAA13376.1	Similar to Schistosoma mansoni amino acid permease (L25068).		431	e-120
				AAH28216.1	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 6		431	e-120
AK018130								
BAB31085.1	Mm.5202	U:(C-D) 2.13		D59433	C. elegans protein Z37093 homolog [imported]		739	0
				BAA13212.1	similar to C.elegans protein (Z37093)		739	0
				AAC03237.1	D1013901		739	0
				XP_037574.1	similar to PTPL1-associated RhoGAP 1		739	0
				AAN04658.1	minor histocompatibility antigen HA-1		739	0
				AAH35564.1	Similar to PTPL1-associated RhoGAP 1		739	0
				NP_004806.1	PTPL1-associated RhoGAP 1		278	2e-74
				E59430	PTPL1-associated RhoGAP protein 1 [imported]		278	2e-74
				AAB81012.1	PTPL1-associated RhoGAP		278	2e-74
				NP_057657.1	Gem-interacting protein		265	2e-70
				D59435	Gem-interacting protein [imported]		265	2e-70
				AAF61330.1	AF132541_1 Gem-interacting protein		265	2e-70
AK014320								
BAB29271.1	Mm.30114	U:(C-D) 2.12		AAL14103.1	AF391100_1 alsin		1569	0
				BAB13389.2	KIAA1563 protein		1569	0
				NP_065970.1	alsin		1569	0
				BAB69014.1	long form		1569	0
				NP_667340.1	hypothetical protein LOC259173		244	5e-64
				BAC04237.1	unnamed protein product		244	5e-64
				BAB84944.1	FLJ00189 protein		244	9e-64

AK014599			U:(C-D) 2.12		AC006029_1 Similar to Sperm Surface Protein PH-20; Similar to P38568 (PID:585674)		
BAB29454.1	Mm.66017			AAD43186.1	hyaluronoglucosaminidase 4	749	0
				NP_036401.1	hyaluronidase 4	749	0
				AAC98883.1	hyaluronidase 4	749	0
					sperm adhesion molecule 1 isoform 2; sperm surface protein PH-20; hyaluronoglucosaminidase	385	e-106
				NP_694859.1	HYAP_HUMAN Hyaluronidase PH-20 precursor (Sperm surface protein PH-20) (Sperm adhesion molecule 1)	385	e-106
				P38567	sperm adhesion molecule gene SPAM1	385	e-106
				CAA59086.1	sperm adhesion molecule 1 isoform 1; sperm surface protein PH-20; hyaluronoglucosaminidase	385	e-106
				NP_003108.2	hyaluronoglucosaminidase	385	e-106
				AAH26163.1	sperm adhesion molecule 1 (PH-20 hyaluronidase, zona pellucida binding)	385	e-106
				AAC60607.2	PH-20	382	e-105
				S40465	sperm protein PH-20	382	e-105
				AAD24460.1	AF118821_1 hyaluronoglucosaminidase 1 isoform 2	337	9e-92
				AAD53277.1	AF173154_1 hyaluronoglucosaminidase 1 isoform 2	337	9e-92
				NP_009296.1	hyaluronoglucosaminidase 1 isoform 1; hyaluronidase 1; tumor suppressor LUCA-1; plasma hyaluronidase; hyaluronoglucosaminidase	336	1e-91
				NP_149349.2	hyaluronoglucosaminidase 1 isoform 1; hyaluronidase 1; tumor suppressor LUCA-1; plasma hyaluronidase; hyaluronoglucosaminidase	336	1e-91
				NP_695013.1	hyaluronoglucosaminidase 1 isoform 1; hyaluronidase 1; tumor suppressor LUCA-1; plasma hyaluronidase; hyaluronoglucosaminidase	336	1e-91
				AAD04190.1	hyaluronoglucosaminidase 1	336	1e-91
				AAD09137.2	putative tumor suppressor	336	1e-91
				AAH35695.1	hyaluronoglucosaminidase 1	336	1e-91
				JC5584	hyaluronoglucosaminidase (EC 3.2.1.35) 1 precursor	333	7e-91
NM_008969					rostaglandin-endoperoxide synthase 1, isoform 1 precursor; prostaglandin G/H synthase and cyclooxygenase; PGH synthase 1; PG synthetase; prostaglandin synthetase; cyclooxygenase-1; prostaglandin H2 synthetase 1	1043	0
NP_032995.1	Mm.2792	U:(C-D) 2.12		NP_000953.2			

				P23219	PGH1_HUMAN Prostaglandin G/H synthase 1 precursor (Cyclooxygenase -1) (COX-1) (Prostaglandin-endoperoxide synthase 1) (Prostaglandin H2 synthase 1) (PGH synthase 1) (PGHS-1) (PHS 1)	1043	0
				JH0259	prostaglandin-endoperoxide synthase (EC 1.14.99.1) 1 precursor	1043	0
				AAA03630.1	prostaglandin endoperoxide synthase	1043	0
				AAB21215.1	prostaglandin endoperoxide synthase; cyclooxygenase	1043	0
				AAB22217.1	prostaglandin G/H synthase; PGG/HS	1043	0
				AAL33601.1	AF40204_1 prostaglandin-endoperoxide synthase 1	1043	0
				AAH29840.1	Unknown (protein for MGC:34214)	1043	0
				AAA36439.1	prostaglandin-endoperoxide synthase-1	1038	0
				NP_542158.1	prostaglandin-endoperoxide synthase 1, isoform 2 precursor; prostaglandin G/H synthase and cyclooxygenase; PGH synthase 1; PG synthetase; prostaglandin synthetase; cyclooxygenase-1; prostaglandin H2 synthetase 1	956	0
				AAB22216.1	prostaglandin G/H synthase; PGG/HS	956	0
				NP_000954.1	prostaglandin-endoperoxide synthase 2 precursor; prostaglandin G/H synthase and cyclooxygenase; cyclooxygenase-2; endoperoxide synthase type II; prostaglandin H synthase type 2; prostaglandin synthase-2; PG synthetase	729	0
				P35354	PGH2_HUMAN Prostaglandin G/H synthase 2 precursor (Cyclooxygenase -2) (COX-2)(Prostaglandin-endoperoxide synthase 2) (Prostaglandin H2 synthase 2) (PGH synthase 2) (PGHS-2) (PHS II)	729	0
				AA57317.1	cyclooxygenase-2	729	0
				BAA05698.1	prostaglandin endoperoxide synthase-2	729	0
				CAB41240.1	PTGS2 (prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase))	729	0
				AAH13734.1	AAH13734 prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	729	0
				A46150	prostaglandin-endoperoxide synthase (EC 1.14.99.1) 2 precursor	729	0
				AAA58433.1	cyclooxygenase-2	729	0
				AAA35803.1	endoperoxide synthase type II	727	0
				AAN52932.1	cyclooxygenase 2b	380	e-105

NM_010225 NP_034355.1	Mm.6260	U:(C-D) 2.11	NP_001443.1	forkhead box F2; forkhead (Drosophila)-like 6	521	e-147
			Q12947	FXF2_HUMAN Forkhead box protein F2 (Forkhead-related protein FKHL6) (Forkhead-related transcription factor 2) (FREAC-2) (Forkhead-related activator-2)	521	e-147
			T09474	forkhead protein FREAC-2	521	e-147
			AAC32226.1	forkhead protein FREAC-2	521	e-147
			AAD19875.1	forkhead transcription factor	521	e-147
			2208384B	transcription factor FREAC-2	508	e-143
			NP_001442.1	forkhead box F1; forkhead (Drosophila)-like 5; Forkhead, drosophila, homolog-like 5; forkhead-related activator 1 [Homo sapiens]	251	3e-66
			Q12946	FXF1_HUMAN Forkhead box protein F1 (Forkhead-related protein FKHL5) (Forkhead-related transcription factor 1) (FREAC-1) (Forkhead-related activator-1)	251	3e-66
			AAC50399.1	FREAC-1	251	3e-66
			AAC61576.1	forkhead transcription factor	251	3e-66
			2208384A	transcription factor FREAC-1	251	3e-66
NM_028770 NP_083046.1	Mm.3338 5	U:(C-D) 2.1	XP_096612.2	similar to RIKEN cDNA 1200016G03	561	e-159
			CAB76832.1	cytokeratin	270	6e-72
			NP_004684.1	cytokeratin type II	270	1e-71
			CAA76730.1	cytokeratin type II	270	1e-71
			AAH24292.1	keratin 5 (epidermolysis bullosa simplex, Dowling-Meara/Kobner/Weber-Cockayne types)	261	5e-69
			AAA36145.1	keratin K5	260	7e-69
			NP_000415.1	keratin 5; Keratin-5; 58 kda cytokeratin; keratin, type II cytoskeletal 5; cytokeratin 5	260	7e-69
			P13647	K2C5_HUMAN Keratin, type II cytoskeletal 5 (Cytokeratin 5) (K5) (CK 5) (58 kDa cytokeratin)	260	7e-69
			A29904	keratin 5, type II, epidermal	260	7e-69
			AAA36143.1	keratin type II	260	7e-69
			AAF97931.1	AF274874_1 keratin 5	260	7e-69

				NP_002264.1	keratin 8; Keratin-8	259	1e-68
				CAA52882.1	Keratin 8	259	1e-68
				AAB18966.1	human cytokeratin 8	259	1e-68
				AAH00654.1	AAH00654 keratin 8	259	1e-68
				A34720	keratin 8, type II cytoskeletal	259	1e-68
				P05787	K2C8_HUMAN Keratin, type II cytoskeletal 8 (Cytokeratin 8) (K8) (CK 8)	259	1e-68
				AAA35763.1	cytokeratin 8	259	1e-68
NM_011671	Mm.1444	U:(C-D)		NP_003346.2	uncoupling protein 2	585	e-167
NP_035801.1	13	2.09		P55851	UCP2_HUMAN Mitochondrial uncoupling protein 2 (UCP 2) (UCPH)	585	e-167
				AAC51336.1	UCP2	585	e-167
				AAC39690.1	uncoupling protein 2	585	e-167
				AAD21151.1	uncoupling protein-2	585	e-167
				AAH11737.1	AAH11737 uncoupling protein 2 (mitochondrial, proton carrier)	585	e-167
				AAB53091.1	uncoupling protein homolog	583	e-166
				CAA11402.1	uncoupling protein 2	583	e-166
				AAB48411.1	uncoupling protein-2	583	e-166
				NP_003347.1	uncoupling protein 3, isoform UCP3L	451	e-127
				P55916	UCP3_HUMAN Mitochondrial uncoupling protein 3 (UCP 3)	451	e-127
				JC5522	uncoupling protein UCP3, mitochondrial	451	e-127
				AAC51367.1	UCP3	451	e-127
				AAC51369.1	uncoupling protein 3	451	e-127
				AAC51767.1	uncoupling protein-3	451	e-127
				AAG02284.1	AF050113_1 uncoupling protein-3	451	e-127
				AAC18822.1	uncoupling protein 3	445	e-125
				AAC51785.1	uncoupling protein 3	432	e-121
				NP_073714.1	uncoupling protein 3, isoform UCP3S	392	e-109
				AAC51356.1	UCP3S	392	e-109

				NP_068605.1	uncoupling protein 1; mitochondrial brown fat uncoupling protein	353	2e-97
				G01858	uncoupling protein 1, mitochondrial	353	2e-97
				AAA85271.1	uncoupling protein	353	2e-97
				P25874	UCP1_HUMAN Mitochondrial brown fat uncoupling protein 1 (UCP 1) (Thermogenin)	350	2e-96
				CAA36214.1	uncoupling protein	250	2e-96
				AAH08392.1	AAH08392 Similar to uncoupling protein 3 (mitochondrial, proton carrier)	206	5e-53
NM_011933 NP_036063.1	Mm.3576 0	U:(C-D) 2.09		NP_065715.1	peroxisomal 2,4-dienoyl-CoA reductase	466	e-131
				CAB92744.1	c359F1.1 (novel protein (ortholog of mouse and rat peroxisomal 2,4-dienoyl-coA reductase (PDCR, DCR-AKL)))	466	e-131
				CAC05664.1	peroxisomal 2,4-dienoyl-CoA reductase	466	e-131
				AAK61231.1	AF006463_11 2,4-dienoyl-Coenzyme A reductase 2 peroxisomal like	466	e-131
				AAH10740.1	AAH10740 2,4-dienoyl CoA reductase 2, peroxisomal	466	e-131
				AAH11968.1	AAH11968 Similar to 2,4-dienoyl CoA reductase 2, peroxisomal	370	e-102
NM_019424 NP_062297.1	Mm.1948 06	U:(C-D) 2.08		AAAL50684.1	AF450133_1 Hermansky-Pudlak syndrome	1065	0
				NP_000186.1	Hermansky-Pudlak syndrome protein; Hermansky-Pudlak syndrome gene; Hermansky-Pudlak syndrome	1064	0
				Q92902	HPS1_HUMAN Hermansky-Pudlak syndrome 1 protein	1064	0
				AAB17869.1	Hermansky-Pudlak syndrome protein	1064	0
				AAB70662.1	Hermansky-Pudlak syndrome protein	998	0
				AAH00175.1	AAH00175 Hermansky-Pudlak syndrome	411	e-114
				AAC52074.1	alternative Hermansky-Pudlak syndrome associated protein	409	e-114
NM_008433 NP_032459.1	Mm.9911	U:(C-D) 2.06		NP_002241.1	intermediate conductance calcium-activated potassium channel protein 1; putative erythrocyte intermediate conductance calcium-activated potassium Gardos channel	607	e-173
				O15554	KCN4_HUMAN Intermediate conductance calcium-activated potassium channel protein 4 (SK4) (KCa4) (IK1) (IKCa1) (Putative Gardos channel)	607	e-173



			calcium-activated potassium channel	607	e-173
			intermediate conductance calcium-activated potassium channel	607	e-173
			hK1	607	e-173
			intermediate conductance calcium-activated potassium channel	607	e-173
			intermediate-conductance calcium-activated potassium channel 1	607	e-173
			potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	607	e-173
			AF395661_1 potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	606	e-173
			small-conductance calcium-activated potassium channel SK3	286	5e-77
			small conductance calcium-activated potassium channel protein 3 isoform a	285	1e-76
			KCN3_HUMAN Small conductance calcium-activated potassium channel protein 3 (SK3) (SKCa3)	285	1e-76
			SK3 protein	285	1e-76
			AF336797_1 small-conductance calcium-activated potassium channel	285	1e-76
			probable calcium-activated potassium channel KCNN3	282	1e-75
			calcium-activated potassium channel	282	1e-75
			KCN1_HUMAN Small conductance calcium-activated potassium channel protein 1 (SK1)	278	2e-75
			small-conductance, calcium-activated potassium channel SK1	278	2e-75
			small-conductance calcium-activated potassium channel 1	278	2e-75
			small conductance calcium-activated potassium channel protein 1	278	2e-75
			AF397175_1 small-conductance calcium-activated potassium channel	280	5e-75
			KCN2_HUMAN Small conductance calcium-activated potassium channel protein 2 (SK2)	279	7e-75
			AF239613_1 apamin-sensitive small-conductance Ca2+-activated potassium channel	279	7e-75
			small conductance calcium-activated potassium channel protein 2 isoform a; apamin-sensitive small-conductance Ca2+-activated potassium channel	279	7e-75

NM_013486 NP_038514.1	Mm.2284 2	U:(C-D) 2.06	RWHUC2	T-cell surface glycoprotein CD2 precursor	255	1e-67
			AAA35571.1	T-cell surface antigen CD2 precursor	255	1e-67
			AAA53095.1	T11 surface antigen	255	1e-67
			CAC14840.1	dJ65N15.1 (CD2 antigen (p50), sheep red blood cell receptor)	255	1e-67
			AAA51946.1	CD2 surface antigen	255	1e-67
			NP_001758.1	CD2 antigen (p50), sheep red blood cell receptor; lymphocyte-function antigen-2	252	8e-67
			P06729	CD2_HUMAN T-cell surface antigen CD2 precursor (T-cell surface antigen T11/Leu-5) (LFA-2) (LFA-3 receptor) (Erythrocyte receptor) (Rosette receptor)	252	8e-67
			AAA51738.1	surface antigen CD2 precursor	252	8e-67
			CAA30721.1	T-cell surface antigen	252	8e-67
			AAH33583.1	CD2 antigen (p50), sheep red blood cell receptor	252	8e-67
NM_029796 NP_084072.1	Mm.1769 46	U:(C-D) 2.06	NP_443204.1	leucine-rich alpha-2-glycoprotein	330	3e-90
			P02750	A2GL_HUMAN Leucine-rich alpha-2-glycoprotein precursor (LRG)	330	3e-90
			AAK95527.1	AF403428_1 leucine-rich alpha-2-glycoprotein	330	3e-90
			NBHUA2	leucine-rich alpha-2-glycoprotein	329	6e-90
			AAH34389.1	leucine-rich alpha-2-glycoprotein	327	2e-89
X71479 CAA50585.1	NULL	U:(C-D) 2.06	CAA50586.1	cytochrome P450	268	2e-72
			NP_000769.1	cytochrome P450, subfamily IVA, polypeptide 11; fatty acid omega-hydroxylase; P450HL-omega; alkane-1 monooxygenase; lauric acid omega-hydroxylase	267	4e-72
			I53015	fatty acid omega-hydroxylase (EC 1.14.15.-) cytochrome P450 4A11	267	4e-72
			AAB29502.1	fatty acid omega-hydroxylase; CYP4A11	267	4e-72
			I65981	fatty acid omega-hydroxylase (EC 1.14.15.-) cytochrome P450 4A11	267	4e-72
			AAB29503.1	fatty acid omega-hydroxylase; CYP4A11v	267	4e-72
			Q02928	CP4Y_HUMAN Cytochrome P450 4A11 precursor (CYP4A11) (Fatty acid omega-hydroxylase) (P-450 HK omega) (Lauric acid omega-hydroxylase) (CYP4A1I) (P450-HL-omega)	265	2e-71

			JX0331	laurate omega-hydroxylase (EC 1.14.15.3) cytochrome P450 4A11 (HL24)	265	2e-71
			AAA58436.1	cytochrome P450	265	2e-71
			BAA05491.1	fatty acids omega-hydroxylase (cytochrome P450HL omega)	265	2e-71
			1908216A	fatty acid omega-hydroxylase (cytochrome P450 4A)	265	2e-71
			BAA02864.1	fatty acid omega-hydroxylase	265	2e-71
			AAF76722.1	AF208532_1 fatty acid omega-hydroxylase CYP4A11	261	2e-70
			CAB72105.1	dJ18D14.4 (cytochrome P450, subfamily IVA, polypeptide 11)	253	6e-68
			AAH28102.1	Unknown (protein for MGC:40051)	202	1e-52
			BAC05226.1	unnamed protein product	202	1e-52
			BAC03751.1	unnamed protein product	202	1e-52
NM_019935 NP_064319.1	Mm.3832 3	U:(C-D) 2.05 U:(IR-D) 2.41	O14753	OVO1_HUMAN Putative transcription factor Ovo-like 1 (hOvo1)	468	e-131
			NP_004552.1	OVO-like 1 binding protein; putative transcription factor OVO-like 1; ovo (Drosophila) homolog-like 1	367	e-101
			AAB72084.1	OVO-like 1 binding protein	367	e-101
			NP_067043.1	zinc finger protein 339; ovo-like 2 (Drosophila)	275	3e-73
			BAB14002.1	unnamed protein product	275	3e-73
			Q9BRP0	Z339_HUMAN Zinc finger protein 339	271	2e-72
			AAH06148.1	AAH06148 putative zinc finger protein from EUROIMAGE 566589	271	2e-72
			CAB45151.1	hypothetical protein, similar to (AF134804) putative zinc finger transcription factor OVO1 [Mus musculus]	238	3e-62
NM_012006 NP_036136.1	Mm.1978	U:(C-D) 2.05	XP_170752.1	similar to peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase ; putative protein	602	e-172
			P49753	PTE2_HUMAN Peroxisomal acyl-coenzyme A thioester hydrolase 2 (Peroxisomal long-chain acyl-coA thioesterase 2) (ZAP128)	600	e-171
			JC7367	second peroxisomal thioesterase	600	e-171
			AAF97985.1	peroxisomal long-chain acyl-coA thioesterase	600	e-171

				AAH04436.1	AAH04436 Unknown (protein for MGC:3983)	600	e-171
				AAH06500.1	AAH06500 Unknown (protein for MGC:2366)	600	e-171
				NP_006812.2	peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase ; putative protein	599	e-171
				AAH06335.1	AAH06335 peroxisomal long-chain acyl-coA thioesterase	599	e-171
				BAA91989.1	unnamed protein product	598	e-171
				NP_689544.1	hypothetical protein FLJ31235	494	e-139
				BAC04313.1	unnamed protein product	494	e-139
				AAC42007.1	ORF; putative	405	e-113
				XP_090885.1	similar to Peroxisomal acyl-coenzyme A thioester hydrolase 2 (Peroxisomal long-chain acyl-coA thioesterase 2) (ZAP128)	280	4e-75
				NP_001692.1	bile acid Coenzyme A: amino acid N-acyltransferase; glycine N-choyltransferase	265	2e-70
				A53965	bile acid-CoA amino acid N-acyltransferase	265	2e-70
				AAC37550.1	bile acid CoA: Amino acid N-acyltransferase	265	2e-70
				AAH09567.1	AAH09567 bile acid Coenzyme A: amino acid N-acyltransferase (glycine N-choyltransferase)	265	2e-70
AK004963							
BAB23703.1	Mm.186	U:(C-D) 2.04		NP_055419.1	Tax interaction protein 1	243	4e-64
				AAB84248.2	Tax interaction protein 1	243	4e-64
				AAG44368.1	AF234997_1 glutaminase-interacting protein 3	243	4e-64
				AAK69111.1	AF277318_1 tax-interacting protein 1	243	4e-64
				AAH23980.1	Tax interaction protein 1	243	4e-64
				AAF43104.1	TIP1	228	2e-59
AK008849							
BAB25928.1	Mm.45435	U:(C-D) 2.04		NP_079119.2	duodenal cytochrome b; hypothetical protein FLJ23462	391	e-109
				CAB66628.1	hypothetical protein	391	e-109
				BAB15661.1	unnamed protein product	386	e-107

					XP_166224.2	similar to data source:SPTR, source key:Q9H0Q8, evidence:ISS-homolog to	196	6e-50
					NP_705839.1	HYPOTHETICAL 31.6 KDA PROTEIN-putative	196	6e-50
					BAC11698.1	hypothetical protein MGC20446	196	6e-50
NM_008532						unnamed protein product		
NP_032558.1	Mm.4259	U:(C-D) 2.03			P16422	TTD1_HUMAN Tumor-associated calcium signal transducer 1 precursor (Major gastrointestinal tumor-associated protein GA733-2) (Epithelial cell surface antigen) (Epithelial glycoprotein) (EGP) (Adenocarcinoma-associated antigen) (KSA) (KS 1/4 antigen) (Cell surface glycoprotein Trop-1)	446	e-125
					CAA32870.1	KSA preproantigen peptide	446	e-125
					AAA36151.1	adenocarcinoma-associated antigen precursor (KSA)	446	e-125
					AAA59543.1	KS1/4 antigen	446	e-125
					NP_002345.1	tumor-associated calcium signal transducer 1 precursor; membrane component, chromosome 4, surface marker (35kD glycoprotein); MK-1 antigen; antigen identified by monoclonal antibody AUA1	446	e-125
					B48149	epithelial glycoprotein antigen GA733-2 precursor	446	e-125
					AAA35861.1	carcinoma-associated antigen GA733-2	446	e-125
					AAB00775.1	carcinoma-associated antigen GA733-2	446	e-125
					AAH14785.1	tumor-associated calcium signal transducer 1	446	e-125
					AAA35723.1	epithelial glycoprotein (EGP) precursor	444	e-124
					A48149	carcinoma-associated antigen GA733-1 precursor	265	2e-70
					CAA31781.1	GA733-1 protein (AA 1-323)	265	2e-70
					CAA54801.1	gp50/TROP-2	265	2e-70
					AAH09409.1	Unknown (protein for MGC:10655)	265	2e-70
					NP_002344.1	tumor-associated calcium signal transducer 2 precursor; membrane component, chromosome 1, surface marker 1 (40kD glycoprotein, identified by monoclonal antibody GA733); epithelial glycoprotein-1	263	6e-70
					CAA54799.1	gp50/Trop-2	263	6e-70
					P09758	TTD2_HUMAN Tumor-associated calcium signal transducer 2 precursor (Pancreatic carcinoma marker protein GA733-1) (Cell surface glycoprotein Trop-2)	262	1e-69
					AAA52505.1	GA733-1 protein precursor	262	1e-69



			S27002	phospholipase C (EC 3.1.4.3), phosphatidylinositol-specific	1663	0
			CAA78903.1	phospholipase c	1663	0
			NP_056007.1	phospholipase C, beta 1 (phosphoinositide-specific); phosphoinositide-specific phospholipase C-beta 1; phospholipase C beta 1; phospholipase C, beta 1 (phosphoinositide-specific)	1197	0
			Q9NQ66	PIB1_HUMAN 1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase beta (PLC-beta-1) (Phospholipase C-beta-1) (PLC-I) (PLC-154)	1197	0
			CAB98142.1	phospholipase C-beta-1a	1197	0
			CAB98143.1	phospholipase C-beta-1b	1192	0
			AAF86613.1	phospholipase C beta 1	1154	0
			BAA25507	KIAA0581 protein	1047	0
			NP_004564.1	phospholipase C, beta 2	934	0
			Q00722	PIB2_HUMAN 1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase beta 2 (PLC-beta-2) (Phospholipase C-beta-2)	934	0
			A43346	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase (EC 3.1.4.11) beta-2	934	0
			AAA36453.1	phospholipase C-beta-2	934	0
			T46339	hypothetical protein DKFZp434A0814.1	885	0
			CAB70666.1	hypothetical protein	885	0
NM_010129 NP_034259.1	Mm.2082 9	U:(C-D) 2	NP_001416.1	epithelial membrane protein 3	250	1e-66
			P54852	EMP3_HUMAN Epithelial membrane protein-3 (EMP-3) (YMP protein) (Hematopoietic neural membrane protein) (HNMP-1)	250	1e-66
			AAC50920.1	YMP	250	1e-66
			AAC51730.1	hematopoietic neural membrane protein	250	1e-66
			AAH09718.1	AAH09718 epithelial membrane protein 3	250	1e-66
			JC5045	epithelial membrane protein 3	244	6e-65
			CAA64394.1	epithelial membrane protein-3	244	6e-65
NM_011644 NP_035774.1	Mm.8361 5	U:(C-D) 2	NP_004612.2	transient receptor potential cation channel, subfamily C, member 6; transient receptor potential channel 6	427	e-119

				Q9Y210	TRP6_HUMAN Short transient receptor potential channel 6 (TrpC6)	427	e-119
				CAA06943.1	transient receptor potential protein	427	e-119
				AAC63289.2	transient receptor potential protein 6	427	e-119
				CAC01684.1	transient receptor potential channel 6	427	e-119
				NP_003296.1	transient receptor potential cation channel, subfamily C, member 3; transient receptor potential channel 3	421	e-117
				Q13507	TRP3_HUMAN Short transient receptor potential channel 3 (TrpC3) (Htrp3)	421	e-117
				CAA74083.1	transient receptor potential related channel 3 protein	421	e-117
				AAC51653.1	calcium influx channel	421	e-117
				NP_065122.1	putative capacitative calcium channel	411	e-114
				Q9HCX4	TRP7_HUMAN Short transient receptor potential channel 7 (TrpC7) (TRP7 protein)	441	e-114
				CAC03489.1	putative capacitative calcium channel	411	e-114
				CAD19069.1	short transient receptor potential channel 7	409	e-113
				AAF22928.1	AF063823_1 trp-related protein 4 truncated variant beta	369	e-101
				AAL24550.1	AF421359_1 transient receptor potential channel 4 beta splice variant	369	e-101
				AAL24551.1	AF421360_1 transient receptor potential channel 4 epsilon splice variant	369	e-101
				NP_057263.1	transient receptor potential 4; transient receptor potential channel 4	369	e-101
				Q9UBN4	TRP4_HUMAN Short transient receptor potential channel 4 (TrpC4) (trp-related protein 4) (hTrp-4) (hTrp4)	369	e-101
				AAD51736.1	AF175406_1 transient receptor potential 4	369	e-101
				AAF22927.1	AF063822_1 trp-related protein 4	369	e-101
				AAL24549.1	AF421358_1 transient receptor potential channel 4 alpha splice variant	369	e-101
				AAF22929.1	AF063824_1 trp-related protein 4 truncated variant delta	369	e-101
				NP_036603.1	transient receptor potential cation channel, subfamily C, member 5; transient receptor potential channel 5	359	2e-98
				Q9UL62	TRP5_HUMAN Short transient receptor potential channel 5 (TrpC5) (Htrp-5) (Htrp5)	359	2e-98
				AAF00002.1	AF054568_1 transient receptor potential calcium channel 5	359	2e-98
				CAC01686.1	transient receptor potential channel 6, variant delta377-431	333	1e-90





Subtable 1C: Mixed Genes and Proteins

Mouse Gene Protein	Unigene	Behavior	Human Proteins	Human Protein Name	Score (bits)	E-value
NM_011369 NP_035499.1	Mm.37801	U:(C-IR) 2.88 F:(IR-D) -2.63	NP_079021.2	likely ortholog of mouse Shc SH2-domain binding protein 1; hypothetical protein FLJ22009	1004 0	
			AAH30699.1	Unknown (protein for MGC:26900)	1004 0	
			BAB71049.1	unnamed protein product	1003 0	
			XP_015700.2	similar to Shc SH2-domain binding protein 1	632 0	
			BAB15208.1	unnamed protein product	630 e-180	
			AAH00960.1	AAH00960 Unknown (protein for IMAGE:3451160)	615 e-176	
			AAG45336.1	GE36	230 8E-60	
			NP_112195.1	chromosome 1 open reading frame 14; GE36 gene	228 2E-59	
			AAG60617.1	AF288398_1 C1orf14	228 2E-59	
			AAG60616.1	AF288397_1 C1orf14	204 6E-52	
NM_015810 NP_056625.1	Mm.859	U:(C-IR) 2.74 F:(IR-D) -3.23	Q9UHN1	DPG2_HUMAN DNA polymerase gamma subunit 2, mitochondrial precursor (Mitochondrial DNA polymerase accessory subunit) (PolG-beta) (MTPoIB) (DNA polymerase gamma accessory 55 kDa subunit) (p55)	712 0	
			AAD50382.1	AF142992_1 DNA polymerase gamma accessory subunit	712 0	
			AAD56640.1	AF177201_1 mitochondrial DNA polymerase accessory subunit precursor	711 0	
			AAH09194.1	AAH09194 Unknown (protein for MGC:15231)	710 0	
			AAD56542.1	AF184344_1 DNA polymerase accessory subunit precursor	707 0	
			NP_009146.1	polymerase (DNA directed), gamma 2, accessory subunit; mitochondrial DNA polymerase, accessory subunit	600 e-171	
			AAC51321.1	mitochondrial DNA polymerase accessory subunit precursor	600 e-171	
NM_007659 NP_031685.1	Mm.4761	U:(C-IR) 2.72 F:(IR-D) -2.86	NP_001777.1	cell division cycle 2 protein, isoform 1; cell division control protein 2 homolog; cyclin-dependent kinase 1; p34 protein kinase; cell cycle controller CDC2	577 e-164	
			P06493	CDC2_HUMAN Cell division control protein 2 homolog (p34 protein kinase) (Cyclin-dependent kinase 1) (CDK1)	577 e-164	

			A29539	protein kinase (EC 2.7.1.37) cdc2	577	e-164
			CAA28963.1	CDC2 polypeptide (CDC2) (AA 1-297)	577	e-164
			CAA68376.1	CDC2 protein (AA 1-297)	577	e-164
			AAH14563.1	Similar to cell division cycle 2, G1 to S and G2 to M	577	e-164
			AAM34793.1	AF512554_1 cell division cycle 2, G1 to S and G2 to M	577	e-164
			1306392A	gene CDC2	577	e-164
			NP_203698.1	cell division cycle 2 protein, isoform 2; cell division control protein 2 homolog; cyclin-dependent kinase 1; p34 protein kinase	409	e-114
			BAA26001.1	CDC2 delta T	409	e-114
			NP_001249.1	cyclin-dependent kinase 3	393	e-109
			Q00526	CDK3_HUMAN Cell division protein kinase 3	393	e-109
			S23382	protein kinase (EC 2.7.1.37) cdk	393	e-109
			CAA47001.1	serine/threonine protein kinase [Homo sapiens]	393	e-109
			CAA43807.1	cell division kinase. CDC2 homolog	390	e-108
			NP_001789.2	cyclin-dependent kinase 2, isoform 1; cdc2-related protein kinase; cell division kinase 2; p33 protein kinase	389	e-108
			P24941	CDK2_HUMAN Cell division protein kinase 2 (p33 protein kinase)	389	e-108
			A41227	protein kinase (EC 2.7.1.37) cdk2	389	e-108
			1KE5	A Chain A, Cdk2 Complexed With N-Methyl-4-[[[(2-Oxo-1,2-Dihydro-3h-Indol-3-Ylidene)methyl]amino}benzenesulfonamide	389	e-108
			1KE6	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With N-Methyl-4-[2-(7-Oxo-6,7-Dihydro-8h-[1,3]thiazolo[5,4-E]indol-8-Ylidene)hydrazino]phenyl]methanesulfonamide	389	e-108
			1KE7	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With 3-[[[(2,2-Dioxido-1,3-Dihydro-2-Benzothien-5-Yl)amino]methylene]-5-(1,3-Oxazol-5-Yl)-1,3-Dihydro-2h-Indol-2-One	389	e-108
			1KE8	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With 4-[[[(2-Oxo-1,2-Dihydro-3h-Indol-3-Ylidene)methyl]amino}-N-(1,3-Thiazol-2-Yl)benzenesulfonamide	389	e-108
			1KE9	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With 3-[[4-[[[amino(imino)methyl]aminosulfonyl]amino]methylene]-2-Oxo-2,3-Dihydro-1h-Indole	389	e-108
			1FIN	A Chain A, Cyclin A - Cyclin-Dependent Kinase 2 Complex	389	e-108
			1FIN	C Chain C, Cyclin A - Cyclin-Dependent Kinase 2 Complex	389	e-108

1FVV			C Chain C, The Structure Of Cdk2CYCLIN A IN COMPLEX WITH AN OXINDOLE Inhibitor	389 e-108
1FVV			A Chain A, The Structure Of Cdk2CYCLIN A IN COMPLEX WITH AN OXINDOLE Inhibitor	389 e-108
1HCL			Human Cyclin-Dependent Kinase 2	389 e-108
1HCK			Human Cyclin-Dependent Kinase 2	389 e-108
1F5Q			A Chain A, Crystal Structure Of Murine Gamma Herpesvirus Cyclin Complexed To Human Cyclin Dependent Kinase 2	389 e-108
1BUH			A Chain A, Crystal Structure Of The Human Cdk2 Kinase Complex With Cell Cycle-Regulatory Protein Cks1	389 e-108
1JSV			A Chain A, The Structure Of Cyclin-Dependent Kinase 2 (Cdk2) In Complex With 4-[(6-Amino-4-Pyrimidinyl) Amino]benzenesulfonamide	389 e-108
1JVP			P Chain P, Crystal Structure Of Human Cdk2 (Unphosphorylated) In Complex With Pk049-365	389 e-108
1DI8			A Chain A, The Structure Of Cyclin-Dependent Kinase 2 (Cdk2) In Complex With 4-[3-Hydroxyvanilino]-6,7-Dimethoxyquinazoline	389 e-108
1FVT			A Chain A, The Structure Of Cyclin-Dependent Kinase 2 (Cdk2) In Complex With An Oxindole Inhibitor	389 e-108
1CKP			A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Purvalanol B	389 e-108
1AQ1			Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Staurosporine	389 e-108
1GIH			A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Cdk4 Inhibitor	389 e-108
1G5S			A Chain A, Crystal Structure Of Human Cyclin Dependent Kinase 2 (Cdk2) In Complex With The Inhibitor H717	389 e-108
1DM2			A Chain A, Human Cyclin-Dependent Kinase 2 Complexed With The Inhibitor Hymenialdisine	389 e-108
1F5Q			C Chain C, Crystal Structure Of Murine Gamma Herpesvirus Cyclin Complexed To Human Cyclin Dependent Kinase 2	389 e-108
AAA35667.1			cdc2-related protein kinase	389 e-108
AAH03065.1			cyclin-dependent kinase 2	389 e-108
AAM34794.1			AF512553_1 cyclin-dependent kinase 2	389 e-108
1717387A			cyclin A dependent p33 kinase:SUBUNIT=2	389 e-108

			1E1X	A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Nu6027	389 e-108
			1E1V	A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Nu2058	389 e-108
			1B38	A Chain A, Human Cyclin-Dependent Kinase 2	389 e-108
			1B39	A Chain A, Human Cyclin-Dependent Kinase 2 Phosphorylated On Thr 160	389 e-108
			1E9H	C Chain C, Thr 160 Phosphorylated Cdk2 - Human Cyclin A3 Complex With The Inhibitor Indirubin-5-Sulphonate Bound	387 e-107
			1E9H	A Chain A, Thr 160 Phosphorylated Cdk2 - Human Cyclin A3 Complex With The Inhibitor Indirubin-5-Sulphonate Bound	387 e-107
			1H1P	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu2058	387 e-107
			1H1P	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu2058	387 e-107
			1H1Q	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6094	387 e-107
			1H1Q	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6094	387 e-107
			1H1R	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6086	387 e-107
			1H1R	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6086	387 e-107
			1H1S	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6102	387 e-107
			1H1S	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6102	387 e-107
			1GY3	A Chain A, Pcdk2CYCLIN A IN COMPLEX WITH MGADP, NITRATE AND PEPTIDE Substrate	387 e-107
			1GY3	C Chain C, Pcdk2CYCLIN A IN COMPLEX WITH MGADP, NITRATE AND PEPTIDE Substrate	387 e-107
			1QMZ	A Chain A, Phosphorylated Cdk2-Cyclin A-Substrate Peptide Complex	387 e-107
			1QMZ	C Chain C, Phosphorylated Cdk2-Cyclin A-Substrate Peptide Complex	387 e-107
			CAA43985.1	cdk2	387 e-107
NM_007418	Mm.57205	U:(C-IR) 2.41	P18825	A2AC_HUMAN Alpha-2C-adrenergic receptor (Alpha-2C adrenoceptor) (Subtype C4)	636 0

NP_031444.1	F:(IR-D) -2.1						
		AAG28076.1	AF280399	1 alpha 2C adrenergic receptor		636	0
		BAA02737.1	alpha2CII-adrenergic receptor			634	0
		AAG28077.1	AF280400	1 alpha 2C adrenergic receptor variant		634	0
		NP_000674.1	alpha-2C-adrenergic receptor; alpha2-AR-C4			601	e-171
		A31237	alpha-2C-adrenergic receptor			601	e-171
		AAA35513.1	kidney alpha-2-adrenergic receptor			601	e-171
		AAC78723.1	alpha2-C4-adrenergic receptor			601	e-171
		A34169	alpha-2A-adrenergic receptor			385	e-106
		AAA51665.1	alpha-2 adrenergic receptor old gene name 'ADRA2R'			385	e-106
		NP_000672.2	alpha-2A-adrenergic receptor; platelet type adrenoceptor, alpha-2A; alpha-2A adrenoceptor; alpha-2AAR subtype C10			384	e-106
		P08913	A2AA_HUMAN Alpha-2A adrenergic receptor (Alpha-2A adrenoceptor) (Alpha-2AAR subtype C10)			384	e-106
		AAF91441.1	AF281308	1 alpha 2A adrenergic receptor		384	e-106
		AAG00447.2	adrenergic receptor alpha-2A			384	e-106
		AAK26743.1	alpha-2A adrenergic receptor			384	e-106
		AAK51162.1	alpha-2A adrenergic receptor			384	e-106
		AAK01634.1	AF316894	1 alpha 2A adrenergic receptor		382	e-105
		AAA51664.1	alpha-2-adrenergic receptor old gene name 'ADRA2R'			381	e-105
		AAK01635.1	AF316895	1 alpha 2B adrenergic receptor		358	2E-98
		P18089	A2AB_HUMAN Alpha-2B adrenergic receptor (Alpha-2B adrenoceptor) (Subtype C2)			355	2E-97
		AAB62558.1	alpha2B-adrenergic receptor			355	2E-97
		NP_000673.1	alpha-2B-adrenergic receptor; alpha-2-adrenergic receptor-like 1			258	4E-68
		A37223	alpha-2B-adrenergic receptor			258	4E-68
		AAA51666.1	alpha-2-adrenergic receptor (alpha-2 C2) old gene name 'ADRA2RL1'			258	4E-68
NM_009608	Mm.686	NP_005150.1	actin, alpha, cardiac muscle precursor			764	0
NP_033738.1	U:(C-IR) 2.32 F:(C-D) - 2.42 F:(IR-D) -5.6						
		XP_012405.3	similar to actin, alpha, cardiac			764	0

			P04270	ACTC HUMAN Actin, alpha cardiac	764 0
			ATHUC	actin, cardiac muscle	764 0
			AAB59619.1	alpha-cardiac actin	764 0
			AAH09978.1	AAH09978 actin, alpha, cardiac muscle	764 0
			NP_001091.1	alpha 1 actin precursor; alpha skeletal muscle actin	759 0
			XP_001869.1	similar to Chain B, The X-Ray Crystal Structure Of The Complex Between Rabbit Skeletal Muscle Actin And Latrunculin A At 2.85 A Resolution	759 0
			P02568	ACTS HUMAN Actin, alpha skeletal muscle (Alpha-actin 1)	759 0
			ATHU	actin alpha 1, skeletal muscle	759 0
			AAB59376.1	alpha-actin	759 0
			AAA60296.1	alpha-skeletal actin precursor	759 0
			AAF02694.1	AF182035.1 skeletal muscle alpha-actin precursor	759 0
			AAH12597.1	Similar to actin, alpha 1, skeletal muscle	759 0
			NP_001604.1	alpha 2 actin; alpha-cardiac actin	755 0
			P03996	ACTA HUMAN Actin, aortic smooth muscle (Alpha-actin 2)	755 0
			CAA32064.1	alpha-actin (AA 1-377)	755 0
			AAH17554.1	AAH17554 actin, alpha 2, smooth muscle, aorta	755 0
			ATHUSM	actin alpha 2, aortic smooth muscle	752 0
			AAAS1577.1	alpha-actin	752 0
			NP_001606.1	actin, gamma 2 propeptide; actin, alpha-3	750 0
			P12718	ACTH HUMAN Actin, gamma-enteric smooth muscle (Alpha-actin 3)	750 0
			A40261	actin gamma, enteric smooth muscle	750 0
			CAA34814.1	gamma-actin (AA 1-376)	750 0
			BAA00546.1	enteric smooth muscle gamma-actin	750 0
			AAH12617.1	Similar to actin, gamma 2, smooth muscle, enteric	750 0
			JC5818	gamma-actin	723 0
			NP_001605.1	actin, gamma 1 propeptide; cytoskeletal gamma-actin; actin, cytoplasmic 2	723 0
			P02571	ACTG HUMAN Actin, cytoplasmic 2 (Gamma-actin)	723 0
			ATHUG	actin gamma 1	723 0
			CAA27723.1	gamma-actin	723 0
			AAAS1579.1	gamma-actin	723 0
			AAH00292.1	actin, gamma 1	723 0
			AAH01920.1	actin, gamma 1	723 0
			AAH07442.1	actin, gamma 1	723 0

			AAH09848.1	actin, gamma 1		723	0
			AAH10999.1	Similar to actin, gamma 1		723	0
			AAH12050.1	Similar to actin, gamma 1		723	0
			AAH15005.1	actin, gamma 1		723	0
			AAH15695.1	actin, gamma 1		723	0
			AAH15779.1	actin, gamma 1		723	0
			AAH18774.1	actin, gamma 1		723	0
			NP_001092.1	beta actin; beta cytoskeletal actin		722	0
			P02570	ACTB_HUMAN Actin, cytoplasmic 1 (Beta-actin)		722	0
			ATHUB	actin beta		722	0
			CAA25099.1	beta-actin		722	0
			AAA51567.1	cytoplasmic beta actin		722	0
			AAH01301.1	actin, beta		722	0
			AAH02409.1	actin, beta		722	0
			AAH04251.1	actin, beta		722	0
			AAH09275.1	actin, beta		722	0
			AAH13380.1	actin, beta		722	0
			AAH14861.1	actin, beta		722	0
			AAH16045	actin, beta		720	0
			CAA45026.1	mutant beta-actin (beta'-actin)		718	0
AA510875	Mm.28984	U:(C-IR) 2.21 F:(IR-D) -2.64	NP_004640.1	chromosome 21 open reading frame 33; human HES1 protein, homolog to E.coli and zebrafish ES1 protein		243	9E-65
NP_613067.1			P30042	ES1_HUMAN ES1 protein homolog, mitochondrial precursor (Protein KNP-I) (GT335 protein)		243	9E-65
			JC4913	anti-sigma cross-reacting protein homolog 1 alpha precursor		243	9E-65
			BAA12984.1	KNP-Ia		243	9E-65
			AAC50938.1	GT335		243	9E-65
			AAC50937.1	similar to E. coli SCRP27A and to zebrafish ES1		243	9E-65
			AAH02370.1	ES1 (zebrafish) protein, human homolog of		243	9E-65
			AAH03587.1	ES1 (zebrafish) protein, human homolog of		243	9E-65
			CAA68857.1	HES1		243	9E-65
			BAA95554.1	HES1 protein		243	9E-65



					BAA21138.1	KNP-I alpha protein	243	9E-65
NM_009349	Mm.299	F:(C-IR) -2.85 U:(IR-D) 3.02			AAD04723.1	thioether S-methyltransferase-like; similar to P40936 (PID:g731019)	271	9E-73
NP_033375.1					O95050	INMT_HUMAN Indolethylamine N-methyltransferase (Aromatic alkylamine N-methyltransferase) (Indolamine N-methyltransferase)(Arylamine N-methyltransferase) (Amine N-methyltransferase)	267	2E-71
					AAF18304.1	AF128846 1 indolethylamine N-methyltransferase	267	2E-71
					AAF18306.1	AF128848 1 indolethylamine N-methyltransferase	267	2E-71
					NP_006765.3	indolethylamine N-methyltransferase; thioester S-methyltransferase-like	266	5E-71
					AAF18305.1	AF128847 1 indolethylamine N-methyltransferase	266	5E-71
					AAH33813.	Unknown (protein for IMAGE:5209218)	266	5E-71
					NP_006160.1	nicotinamide N-methyltransferase	239	6E-63
					P40261	NNMT_HUMAN Nicotinamide N-methyltransferase	239	6E-63
					A54060	nicotinamide N-methyltransferase (EC 2.1.1.1)	239	6E-63
					AAA19904.1	nicotinamide N-methyltransferase	239	6E-63
					AAA93158.1	nicotinamide N-methyltransferase	239	6E-63
					AAH00234.1	AAH00234 nicotinamide N-methyltransferase	239	6E-63
NM_019813	Mm.19016	F:(C-IR) -2.71 U:(IR-D) 2.42			Q16643	DREB_HUMAN Drebrin (Developmentally regulated brain protein)	760	0
NP_062787.1					JN0809	drebrin E (clone gDbh13)	760	0
					AAA16256.1	drebrin E2	760	0
					BAA04480.1	drebrin E	760	0
					AAH00283.1	AAH00283 drebrin 1	760	0
					AAH07281.1	AAH07281 drebrin 1	760	0
					AAH07567.1	AAH07567 drebrin 1	760	0
					NP_004386.2	drebrin 1 isoform a; drebrin E; drebrin-1; drebrin E2	759	0
					T14763	hypothetical protein DKFZp434D064.1	704	0
					CAB53683.1	hypothetical protein	704	0
					NP_543157.1	drebrin 1 isoform b; drebrin E; drebrin-1; drebrin E2	703	0

NM_009185	Mm.3988	F:(C-IR) -2.64 U:(IR-D) 2.51	NP_003026.1	TAL1 (SCL) interrupting locus; SCL interrupting locus	1749 0
NP_033211.1			A41685	SIL protein	1749 0
			AAA60550.1	SIL	1749 0
			AAK51418.1	SIL protein	1749 0
			CAB72102.1	dJ18D14.1 (TAL1 (SCL) interrupting locus)	741 0
NM_009665	Mm.7880	F:(C-IR) -2.6 U:(IR-D) 3.96	AAH00171.1	S-adenosylmethionine decarboxylase 1	630 e-180
NP_033795.1					
			NP_001625.1	S-adenosylmethionine decarboxylase 1 precursor	628 e-179
			P17707	DCAM_HUMAN S-adenosylmethionine decarboxylase proenzyme (AdoMetDC) (SamDC) [Contains: S-adenosylmethionine decarboxylase alpha chain; S-adenosylmethionine decarboxylase beta chain]	628 e-179
			DCHUDM	adenosylmethionine decarboxylase (EC 4.1.1.50) precursor	628 e-179
			AAA51716.1	S-adenosylmethionine decarboxylase proenzyme (EC 4.1.1.50) old gene name 'AMD'	628 e-179
			IJL0	B Chain B, Structure Of A Human S-Adenosylmethionine Decarboxylase Self-Processing Ester Intermediate And Mechanism Of Putrescine Stimulation Of Processing As Revealed By The H243a Mutant	623 e-178
			IJL0	A Chain A, Structure Of A Human S-Adenosylmethionine Decarboxylase Self-Processing Ester Intermediate And Mechanism Of Putrescine Stimulation Of Processing As Revealed By The H243a Mutant	623 e-178
			IJEN	A Chain A, Human S-Adenosylmethionine Decarboxylase	499 e-140
			IJEN	C Chain C, Human S-Adenosylmethionine Decarboxylase	499 e-140
			I17C	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Complexed With Methylglyoxal Bis- (Guanyldiazone)	498 e-140
			I172	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Covalently Bound 5'-Deoxy-5'-[n- Methyl-N-(2-Aminoxyethyl) Amino]adenosine	498 e-140

			1179	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Covalently Bound 5'-Deoxy-5'-(3-Hydrazinopropyl)methylamino]adenosine	498 e-140
			117B	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Covalently Bound S-Adenosylmethionine Methyl Ester	498 e-140
			117M	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently One-2'-Amidinohydrazone	474 e-133
			117M	C Chain C, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Complexed With 4-Amidinoindan-1-One-2'-Amidinohydrazone	474 e-133
NM_026599 NP_080875.1	Mm.87428 F:(C-IR) -2.43 U:(IR-D) 2.5	BAB21840.1		KIAA1749 protein	201 2E-51
		NP_116255.1		hypothetical protein FLJ14957	201 2E-51
		BAB5415.1		unnamed protein product	201 2E-51
NM_009519 NP_033545.1	Mm.22182 F:(C-IR) -2.4 U:(C-D) 2.09 U:(IR-D) 2.84	NP_004617.2		wingless-type MMTV integration site family, member 11 precursor	680 0
		O96014		WN11_HUMAN WNT-11 protein precursor	680 0
		BAB72099.1		WNT11	680 0
		CAA73223.1		WNT11	676 0
		CAA74159.1		HWNT1	676 0
		BAC11683.1		unnamed protein product	362 1E-99
		BAC23080.1		WNT4	301 2E-81
		NP_110388.2		wingless-type MMTV integration site family, member 4 precursor; signaling protein WNT-4; WNT-4 protein precursor	301 2E-81
		P56705		WNT4_HUMAN WNT-4 protein precursor	301 2E-81
		AAK51699.1		AF316543 1 signaling protein WNT-4	301 2E-81
		AAG38658.1		WNT4 precursor	296 5E-80

			CAB52601.1	dJ224A6.2 (similar to Mouse Wnt-4 protein)	295	1E-79
			NP_116031.1	wingless-type MMTV integration site family, member 5B precursor; WNT-5B protein precursor	262	1E-69
			NP_110402.2	wingless-type MMTV integration site family, member 5B precursor; WNT-5B protein precursor	262	1E-69
			Q9H1J7	WN5B_HUMAN WNT-5B protein precursor	262	1E-69
			AAH01749.1	AAH01749 Similar to wingless-related MMTV integration site 5B	262	1E-69
			BAB62039.1	WNT5B	262	1E-69
			NP_003383.1	wingless-type MMTV integration site family, member 5A precursor; proto-oncogene Wnt-5A precursor; WNT-5A protein precursor	261	3E-69
			P41221	WN5A_HUMAN WNT-5A protein precursor	261	3E-69
			A48914	proto-oncogene Wnt-5A precursor	261	3E-69
			AAA16842.1	hWNT5	261	3E-69
			AAG38659.1	WNT5b precursor	255	1E-67
AF294617	Mm.19669	F:(C-IR)-2.39	NP_004557.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3	1030	0
AAG02118.1		U:(IR-D) 2.05				
			XP_096349.2	similar to 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3 (6PF-2-K/Fru-2,6-P2ASE brain/placenta-type isozyme) (iPFK-2)	1030	0
			Q16875	F263_HUMAN 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3 (6PF-2-K/Fru-2,6-P2ASE brain/placenta-type isozyme) (iPFK-2) [Includes: 6-phosphofructo-2-kinase ; Fructose-2,6-bisphosphatase ]	1030	0
			BAA08624.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase	1030	0
			AAD08818.1	ubiquitous 6-phosphofructo-2-kinase/fructose 2,6-bisphosphatase	1030	0
			AAL40083.1	L77662 1 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase	1030	0
			AAH40482.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3	1030	0
			2208342A	fructose 6-phosphate 2-kinase/fructose 2,6-bisphosphatase	1030	0
			AAB99795.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase	1028	0
			JC4626	6-phosphofructo-2-kinase (EC 2.7.1.105) / fructose-2, 6-bisphosphate 2-phosphatase (EC 3.1.3.46)	1028	0
			AAC62000.1	inducible 6-phosphofructo-2-kinase/fructose 2,6-bisphosphatase	1005	0
			CAA06605.1	6-phosphofructo-2-kinase	699	0

				O60825	F262 HUMAN 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 2 (6PF-2-K/Fru-2,6-P2ASE heart-type isozyme) (PFK-2/FBPase-2) [Includes: 6-phosphofructo-2-kinase ; Fructose-2,6-bisphosphatase ]	697 0
				NP_006203.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 2; Fructose-2,6-bisphosphatase, cardiac isozyme	688 0
				CAA06606.1	6-phosphofructo-2-kinase	688 0
				BAB19681.1	6-phosphofructo-2-kinase heart isoform	680 0
				AAL99386.1	AF470623.1 PFK2/F26DPase	680 0
				NP_004558.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 4	670 0
				Q16877	F264 HUMAN 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 4 (6PF-2-K/Fru-2,6-P2ASE testis-type isozyme) [Includes: 6-phosphofructo-2-kinase ; Fructose-2,6-bisphosphatase ]	670 0
				BAA18921.1	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase	670 0
				AAD09427.1	testis 6-phosphofructo-2-kinase/fructose 2,6-bisphosphatase	670 0
				AAH10269.1	AAH10269 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 4	670 0
				JC5871	6-phosphofructo-2-kinase (EC 2.7.1.105) / fructose-2,6-bisphosphate 2-phosphatase (EC 3.1.3.46)	669 0
NM_013927 NP_038955.1	Mm.10357 5	F:(C-IR) -2.33 U:(C-D) 3.63 U:(IR-D) 2.84		NP_061971.2	cyclic nucleotide gated channel beta 3; cyclic nucleotide-gated channel, beta 3	910 0
				AAF86274.1	AF272900_1 cone photoreceptor cyclic nucleotide-gated channel beta subunit	910 0
				AAF80179.1	AF228520_1 cone photoreceptor cGMP-gated cation channel beta-subunit	773 0
				Q14028	CNG4_HUMAN Cyclic-nucleotide-gated cation channel 4 (CNG channel 4) (CNG-4) (CNG4) (Cyclic nucleotide-gated cation channel modulatory subunit)	609 e-173
				AAA65620.1	cyclic nucleotide-gated cation channel	609 e-173
				S32538	cGMP-gated cation channel 2, rod	609 e-173
				AAB32607.1	cGMP-gated cation channel subunit 2, cGMP-gated cation channel, subunit beta, hRNCNC2 [human, retinal rod cells, Peptide, 909 aa]	609 e-173
				1912307A	cyclic nucleotide-gated cation channel	609 e-173
				AAB63387.1	cGMP-gated cation channel beta subunit	609 e-173

			NP_001288.1	cyclic nucleotide gated channel beta 1; cyclic nucleotide gated channel (photoreceptor), cGMP gated 3 (gamma)-like	609 e-173
			AAC04830.1	rod photoreceptor CNG-channel beta subunit	609 e-173
			AAAG5619.1	cyclic nucleotide-gated cation channel	598 e-170
			S74179	cyclic nucleotide-gated channel protein	269 3E-71
			NP_001289.1	cyclic nucleotide-gated channel alpha 3	269 3E-71
			Q16281	CNG3_HUMAN Cyclic-nucleotide-gated cation channel alpha 3 (CNG channel alpha 3) (CNG-3) (CNG3) (Cyclic nucleotide gated channel alpha 3) Cone photoreceptor cGMP-gated channel alpha subunit	269 3E-71
			AAC17440.1	cone photoreceptor cGMP-gated channel alpha subunit	269 3E-71
			NP_000078.1	cyclic nucleotide gated channel alpha 1	268 6E-71
			A42161	cGMP-gated cation channel, rod photoreceptor	268 6E-71
			AAAS2010.1	cGMP-gated cation channel protein	268 6E-71
NM_026302	Mm.78718	F:(C-IR)-2.21	NP_057305.1	dynactin 4 (p62); dynactin p62 subunit	886 0
NP_080578.1		U:(IR-D) 2.61			
			XP_041993.1	similar to dynactin 4 (p62); dynactin p62 subunit	886 0
			AAF03896.1	AF195120 1 dynactin p62 subunit	886 0
			BAA91066.1	unnamed protein product	886 0
			AAH26323.1	dynactin 4 (p62)	883 0
			T47143	hypothetical protein DKFZp761J032.1	282 8E-76
			CAB82417.1	hypothetical protein	282 8E-76
NM_007755	Mm.22062	F:(C-IR)-2.2	NP_085097.2	cytoplasmic polyadenylation element binding protein; hypothetical protein FLJ13203 similar to cytoplasmic polyadenylation element binding protein; cytoplasmic polyadenylation element-binding protein	1039 0
NP_031781.1		U:(IR-D) 2.11			
			AAK01239.1	AF329402_1 cytoplasmic polyadenylation element-binding protein long form	1039 0
			AAK01240.1	AF329403_1 cytoplasmic polyadenylation element-binding protein short form	898 0
			AAH35348.1	Similar to cytoplasmic polyadenylation element binding protein	880 0
			BAB14496.1	unnamed protein product	878 0
			NP_055727.1	KIAA0940 protein	207 5E-53

			BAA76784.1	KIAA0940 protein		207	5E-53
			XP_047672.4	similar to RIKEN cDNA 4930447D24		207	6E-53
			BAB21764.1	KIAA1673 protein		207	6E-53
			AAH36899.1	Unknown (protein for MGC:46609)		207	6E-53
			AAH36444.1	Similar to KIAA0940 protein		203	9E-52
NM_008422	Mm.39092	F:(C-IR) -2.17	NP_004968.2	Shaw-related voltage-gated potassium channel protein 3; Kv3.3; voltage-gated potassium channel protein Kv3.3		778	0
NP_032448.1		U:(C-D) 2.07					
		U:(IR-D) 2.33					
			Q14003	KNC3_HUMAN Potassium voltage-gated channel subfamily C member 3 (Potassium channel Kv3.3) (KSHIID)		778	0
			AAC24118.1	Shaw type potassium channel Kv3.3		778	0
			NP_004967.1	Shaw-related voltage-gated potassium channel protein 1; voltage-gated potassium channel protein Kv3.1; potassium voltage-gated channel subfamily C member 1		612	e-175
			P48547	KNC1_HUMAN Potassium voltage-gated channel subfamily C member 1 (Potassium channel Kv3.1) (Kv4) (NGK2)		612	e-175
			A46020	potassium channel KCNC1		612	e-175
			AAB25764.1	voltage-gated potassium channel; NGK2		612	e-175
			NP_004969.2	Shaw-related voltage-gated potassium channel protein 4 isoform a; voltage-gated potassium channel protein Kv3.4		571	e-162
			CAC19684.1	dJ1003J2.3.2 (potassium voltage-gated channel, Shaw-related subfamily, member 4)		571	e-162
			Q03721	CIKG_HUMAN Potassium voltage-gated channel subfamily C member 4 (Potassium channel Kv3.4) (KSHIIC)		571	e-162
			AAA57263.1	potassium channel protein		571	e-162
			NP_720198.1	Shaw-related voltage-gated potassium channel protein 4 isoform b; voltage-gated potassium channel protein Kv3.4		571	e-162
			CAC19683.1	dJ1003J2.3.1 (potassium voltage-gated channel, Shaw-related subfamily, member 4)		571	e-162
			NP_715624.1	Shaw-related voltage-gated potassium channel protein 2 isoform Kv3.2c		556	e-158
			BAC04407.1	unnamed protein product		556	e-158
			NP_631875.1	Shaw-related voltage-gated potassium channel protein 2 isoform Kv3.2b		556	e-158

				AAF268896	1 voltage gated potassium channel Kv3.2b		556	e-158
				AAM81577.1	potassium voltage-gated potassium channel subfamily C member 2		556	e-158
				NP_631874.1	Shaw-related voltage-gated potassium channel protein 2 isoform KV3.2a		556	e-158
				AAF268897	1 voltage gated potassium channel Kv3.2a		556	e-158
NM_011749 NP_035879.1	Mm.417	F:(C-IR) -2.05 U:(IR-D) 2.34		Q9UQR1	Z148_HUMAN Zinc finger protein 148 (Zinc finger DNA binding protein 89) (Transcription factor ZBP-89)		1460	0
				AAC39926.1	zinc finger DNA binding protein 89 kDa		1460	0
				AAL99917.1	AF432210 1 CLL-associated antigen KW-10		1458	0
				NP_068799.1	zinc finger protein 148 (pHZ-52); zinc finger protein 148 (pHZ-52), BERF-1, ZBP-89		1455	0
				CAA15422.1	ZBP-89 protein		1455	0
				A54693	CACCC box-binding protein ht-beta		744	0
				AAA36664.1	CACCC box-binding protein		743	0
				AAH35591.1	Similar to zinc finger protein 148 (pHZ-52)		714	0
				AAB57692.1	zinc finger binding protein homolog		695	0
				CAB70967.1	zinc finger protein		371	e-102
				NP_036614.1	zinc finger protein 281; ZNP-99 transcription factor		371	e-102
				Q9Y2X9	Z281_HUMAN Zinc finger protein 281 (Zinc finger DNA binding protein 99) (Transcription factor ZBP-99) (GC-box-binding zinc finger protein 1)		371	e-102
				JC7089	zinc finger binding protein-99		371	e-102
				AAD21084.1	zinc finger DNA binding protein 99		371	e-102
				CAB70968.1	zinc finger protein		371	e-102
NM_030566 NP_085043.1	Mm.35467	F:(C-IR) -2.05 U:(C-D) 2.62 U:(IR-D) 2.1		NP_079092.1	Fos-related antigen		621	e-177
				BAB15594.1	unnamed protein product		621	e-177
NM_026334	Mm.46408	F:(C-IR)		NP_004181.1	lipase, gastric		663	0



NP_080610.1	-2.04 U:(C-D) 2.14 U:(IR-D) 2.27					
		P07098		LIPG_HUMAN Triacylglycerol lipase, gastric precursor (Gastric lipase) (GL)	663	0
		S07145		triacylglycerol lipase (EC 3.1.1.3) precursor, gastric	663	0
		CAA29413.1		gastric lipase precursor	663	0
		CAA29414.1		gastric lipase precursor	657	0
		1HLG		A Chain A, Crystal Structure Of Human Gastric Lipase	635	0
		1HLG		B Chain B, Crystal Structure Of Human Gastric Lipase	635	0
		G01416		lysosomal acid lipase	474	e-133
		AAB60328.1		lysosomal acid lipase	474	e-133
		CAA83495.1		lysosomal acid lipase	474	e-133
		AAH12287.1		AAH12287 Similar to lipase A, lysosomal acid, cholesterol esterase (Wolman disease)	474	e-133
		S41408		lysosomal acid lipase (EC 3.1.1.-) / sterol esterase (EC 3.1.1.13) precursor	474	e-133
		CAA54026.1		lysosomal acid lipase; sterol esterase	474	e-133
		AAB60327.1		lysosomal acid lipase/cholesteryl ester hydrolase	474	e-133
		NP_000226.1		lipase A precursor; Lipase A, lysosomal acid, cholesterol esterase	474	e-133
		P38571		LICH_HUMAN Lysosomal acid lipase/cholesteryl ester hydrolase precursor (LAL) (Acid cholesteryl ester hydrolase) (Sterol esterase) (Lipase A) (Cholesteryl esterase)	474	e-133
		AAA59519.1		lysosomal acid lipase/cholesteryl esterase	474	e-133
		XP_089555.2		similar to bA30415.1 (novel lipase)	433	e-121
		XP_061222.1		similar to Triacylglycerol lipase, gastric precursor (Gastric lipase) (GL)	431	e-121
		CAC78754.1		bA30415.1 (novel lipase)	428	e-119

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Citation of documents herein is not intended as an admission that any of the documents cited herein is pertinent prior art, or an admission that the cited documents is considered material to the patentability of any of the claims of the present application. All statements as to the date or representation as to the contents of these documents is based on the information available to the applicant and does not constitute any admission as to the correctness of the dates or contents of these documents.

The appended claims are to be treated as a non-limiting recitation of preferred embodiments.

In addition to those set forth elsewhere, the following references are hereby incorporated by reference, in their most recent editions as of the time of filing of this

application: Kay, Phage Display of Peptides and Proteins: A Laboratory Manual; the John Wiley and Sons Current Protocols series, including Ausubel, Current Protocols in Molecular Biology; Coligan, Current Protocols in Protein Science; Coligan, Current Protocols in Immunology; Current Protocols in Human Genetics; Current Protocols in Cytometry; Current Protocols in Pharmacology; Current Protocols in Neuroscience; Current Protocols in Cell Biology; Current Protocols in Toxicology; Current Protocols in Field Analytical Chemistry; Current Protocols in Nucleic Acid Chemistry; and Current Protocols in Human Genetics; and the following Cold Spring Harbor Laboratory publications: Sambrook, Molecular Cloning: A Laboratory Manual; Harlow, Antibodies: A Laboratory Manual; Manipulating the Mouse Embryo: A Laboratory Manual; Methods in Yeast Genetics: A Cold Spring Harbor Laboratory Course Manual; Drosophila Protocols; Imaging Neurons: A Laboratory Manual; Early Development of *Xenopus laevis*: A Laboratory Manual; Using Antibodies: A Laboratory Manual; At the Bench: A Laboratory Navigator; Cells: A Laboratory Manual; Methods in Yeast Genetics: A Laboratory Course Manual; Discovering Neurons: The Experimental Basis of Neuroscience; Genome Analysis: A Laboratory Manual Series ; Laboratory DNA Science; Strategies for Protein Purification and Characterization: A Laboratory Course Manual; Genetic Analysis of Pathogenic

Bacteria: A Laboratory Manual; PCR Primer: A Laboratory Manual; Methods in Plant Molecular Biology: A Laboratory Course Manual ; Manipulating the Mouse Embryo: A Laboratory Manual; Molecular Probes of the Nervous System; Experiments with Fission Yeast: A Laboratory Course Manual; A Short Course in Bacterial Genetics: A Laboratory Manual and Handbook for Escherichia coli and Related Bacteria; DNA Science: A First Course in Recombinant DNA Technology; Methods in Yeast Genetics: A Laboratory Course Manual; Molecular Biology of Plants: A Laboratory Course Manual.

All references cited herein, including journal articles or abstracts, published, corresponding, prior or otherwise related U.S. or foreign patent applications, issued U.S. or foreign patents, or any other references, are entirely incorporated by reference herein, including all data, tables, figures, and text presented in the cited references. Additionally, the entire contents of the references cited within the references cited herein are also entirely incorporated by reference.

Reference to known method steps, conventional methods steps, known methods or conventional methods is not in any way an admission that any aspect, description or embodiment of the present invention is disclosed, taught or suggested in the relevant art.

The foregoing description of the specific embodiments will so fully reveal the general nature of the invention that others can, by applying knowledge within the skill of the art (including the contents of the references cited herein), readily modify and/or adapt for various applications such specific embodiments, without undue experimentation, without departing from the general concept of the present invention. Therefore, such adaptations and modifications are intended to be within the meaning and range of equivalents of the disclosed embodiments, based on the teaching and guidance presented herein. It is to be understood that the phraseology or terminology herein is for the purpose of description and not of limitation, such that the terminology or phraseology of the present specification is to be interpreted by the skilled artisan in light of the

teachings and guidance presented herein, in combination with the knowledge of one of ordinary skill in the art.

Any description of a class or range as being useful or preferred in the practice of the invention shall be deemed a description of any subclass (e.g., a disclosed class with one or more disclosed members omitted) or subrange contained therein, as well as a separate description of each individual member or value in said class or range.

The description of preferred embodiments individually shall be deemed a description of any possible combination of such preferred embodiments, except for combinations which are impossible (e.g, mutually exclusive choices for an element of the invention) or which are expressly excluded by this specification.

If an embodiment of this invention is disclosed in the prior art, the description of the invention shall be deemed to include the invention as herein disclosed with such embodiment excised.

CLAIMS

1. A method of protecting a human subject from progression from a normoinsulinemic state to a  
5 hyperinsulinemic state, or from either to a type II diabetic state, which comprises administering to the subject a protective amount of an agent which is

(1) a polypeptide which is substantially structurally  
10 identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master table 1, subtables 1A and 1C,

15 or

(2) an expression vector encoding the polypeptide of (1) above and expressible in a human cell, under conditions conducive to expression of the polypeptide of (1);

20 where said agent protects said subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

25 2. A method of protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state which comprises administering to the subject a protective amount of an agent which is

30 (1) an antagonist of a polypeptide, occurring in said subject, which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and  
35 human proteins set forth in master table 1, subtable 1B and 1C, or

(2) an anti-sense vector which inhibits expression of said polypeptide in said subject,



where said agent protects said subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

5           3. A method of screening for human subjects who are prone to progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of a  
10   "favorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master  
15   table 1, subtables 1A and 1C,

and directly correlating the level of expression of said marker gene with the propensity to progression in said patient.

20

          4. A method of screening for human subjects who have a propensity for progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body  
25   fluid samples from said subjects to determine the level of expression of an "unfavorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is  
30   selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B and 1C, and inversely correlating the level of expression of said marker gene with the propensity to progression in said patient.

35

5. The method of claims 1 or 3 in which the reference protein is of subtable 1A.

6. The method of claims 1 or 3 in which the reference

protein is of subtable 1B.

7. The method of claim 3 or 4 in which the sample is a muscle tissue sample.

5

8. The method of any one of claims 1-7 in which the reference protein is a human protein.

10

9. The method of any one of claims 1-7 in which the reference protein is a mouse protein.

15

10. The method of any one of claims 3 or 4 in which the level of expression of the marker protein is ascertained by measuring the level of the corresponding messenger RNA.

11. The method of any one of claims 3 or 4 in which the level of expression is ascertained by measuring the level of a protein encoded by said marker gene.

20

12. The method of any one of claims 1-9 in which said polypeptide is at least 80% identical or at least highly conservatively identical to said reference protein.

25

13. The method of any one of claims 1-10 in which said polypeptide is at least 90% identical to said reference protein.

14. The method of any one of claims 1-11 in which said polypeptide is identical to said reference protein.

30

15. The method of any one of claims 1-14 in which the E-value cited for the reference protein in Master Table 1 is not more than  $e^{-6}$ .

35

16. The method of claim 15 in which the E-value cited for the reference protein in Master Table 1 is less than  $e^{-10}$ .

17. The method of claim 17 in which the E value calculated by BLASTN or BLASTX would be less than  $e^{-15}$ , more preferably less than  $e^{-20}$ , still more preferably less than  $e^{-40}$ , even

more preferably less than e-60, considerably more preferably less than e-80, and most preferably less than e-100.

5 18. The method of any of claims 2-17 in which the antagonist is an antibody, or an antigen-specific binding fragment of an antibody.

10 19. The method of any of claims 2-17 in which the antagonist is a peptide, peptoid, nucleic acid, or peptide nucleic acid oligomer.

15 20. The method of any of claims 2-17 in which the antagonist is an organic molecule with a molecular weight of less than 500 daltons.

21. The method of claim 20 in which said organic molecule is identifiable as a molecule which binds said polypeptide by screening a combinatorial library.

20 22. The method of claim 1 or 2 in which the agent is delivered systemically.

25 23. The method of claim 1 or 2 in which the agent is selectively delivered to muscle tissue.

**ABSTRACT OF THE DISCLOSURE**

Mouse genes differentially expressed in comparisons of  
normal vs. hyperinsulinemic, hyperinsulinemic vs. type 2  
5 diabetic, and normal vs. type 2 diabetic muscle by gene chip  
analysis have been identified, as have corresponding human  
genes and proteins. The human molecules, or antagonists  
thereof, may be used for protection against hyperinsulinemia  
or type 2 diabetes, or their sequelae.

10

Figure 1(a)

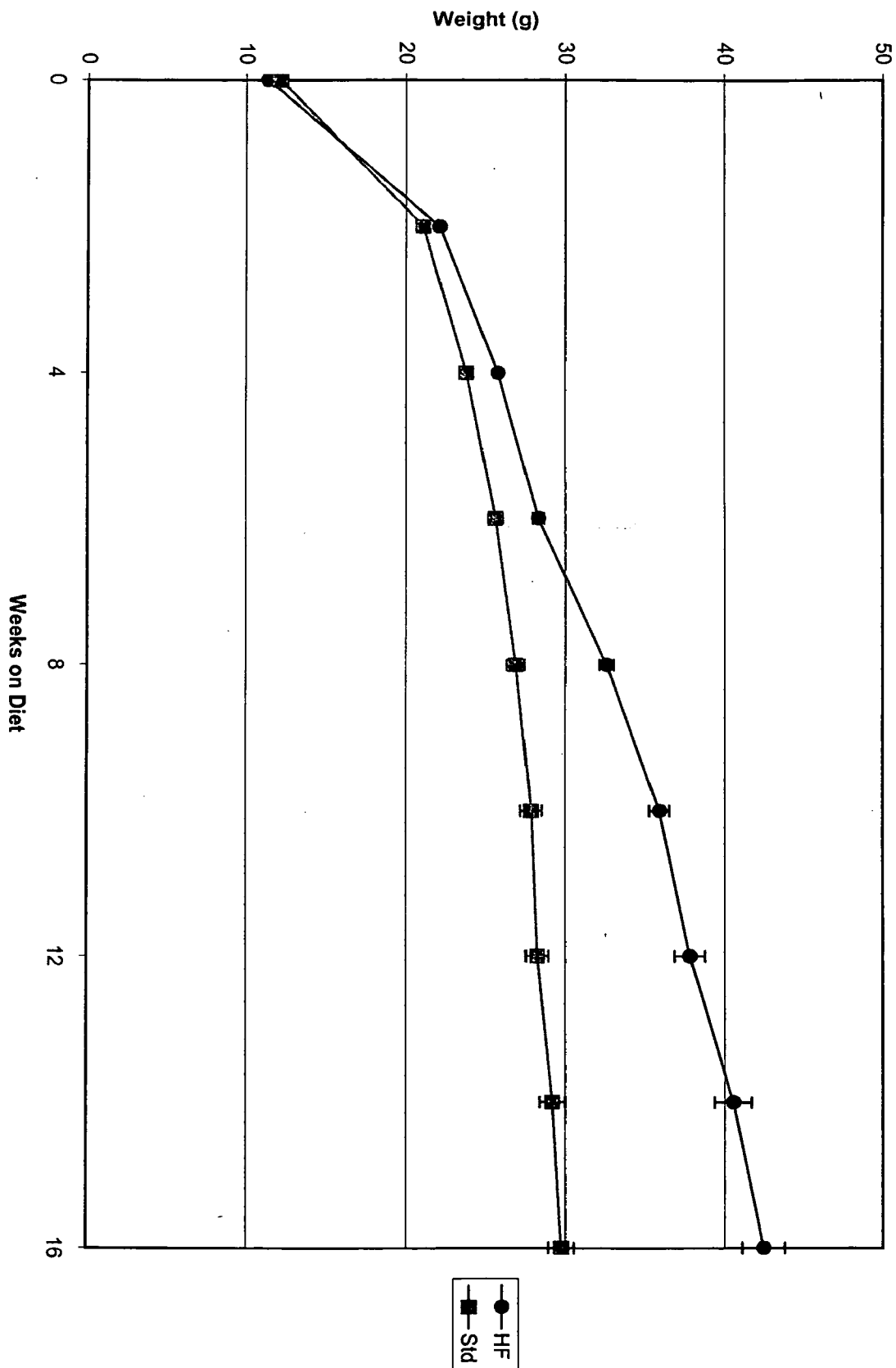


Figure 1(b)

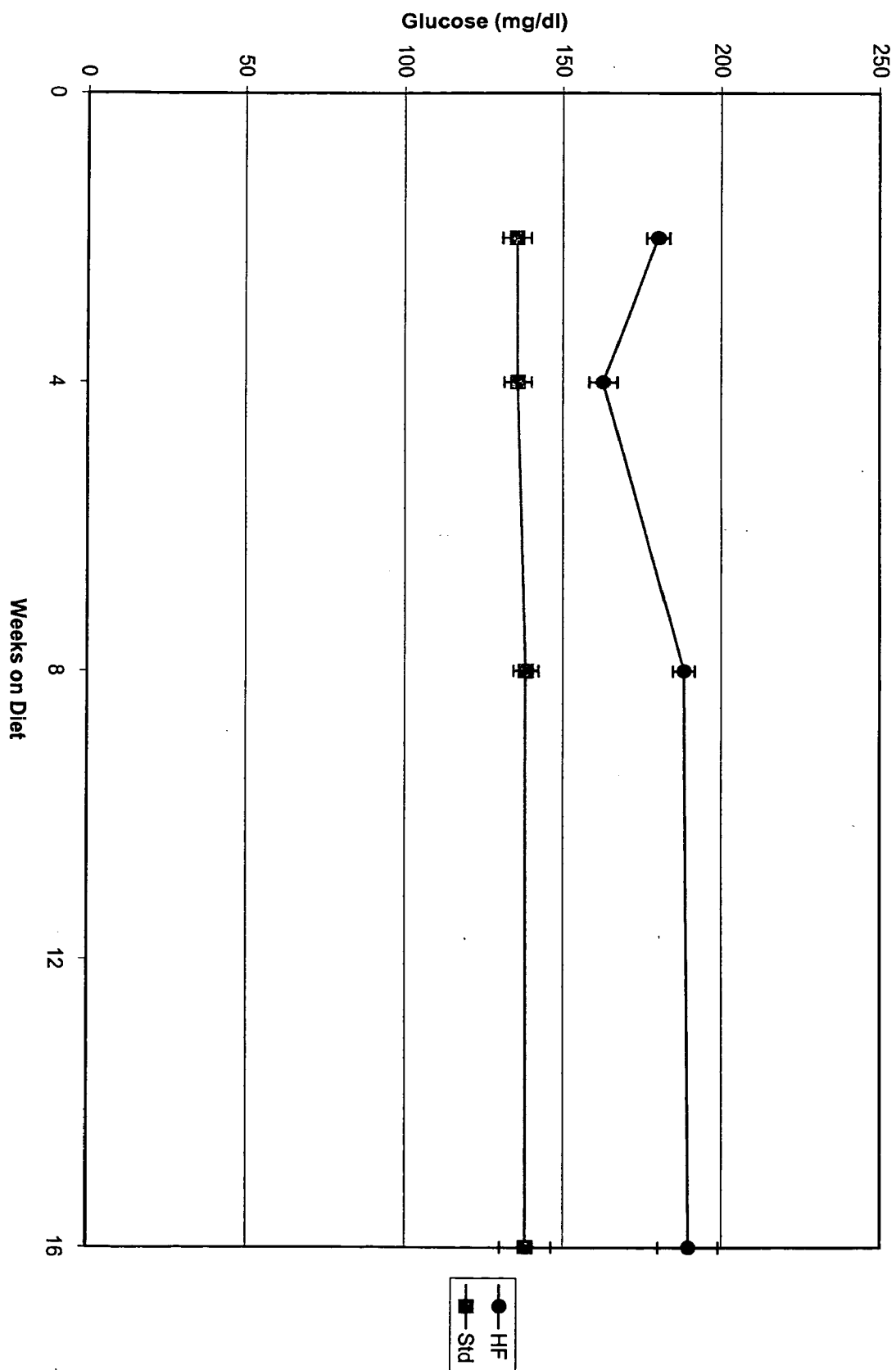


Figure 1(c)

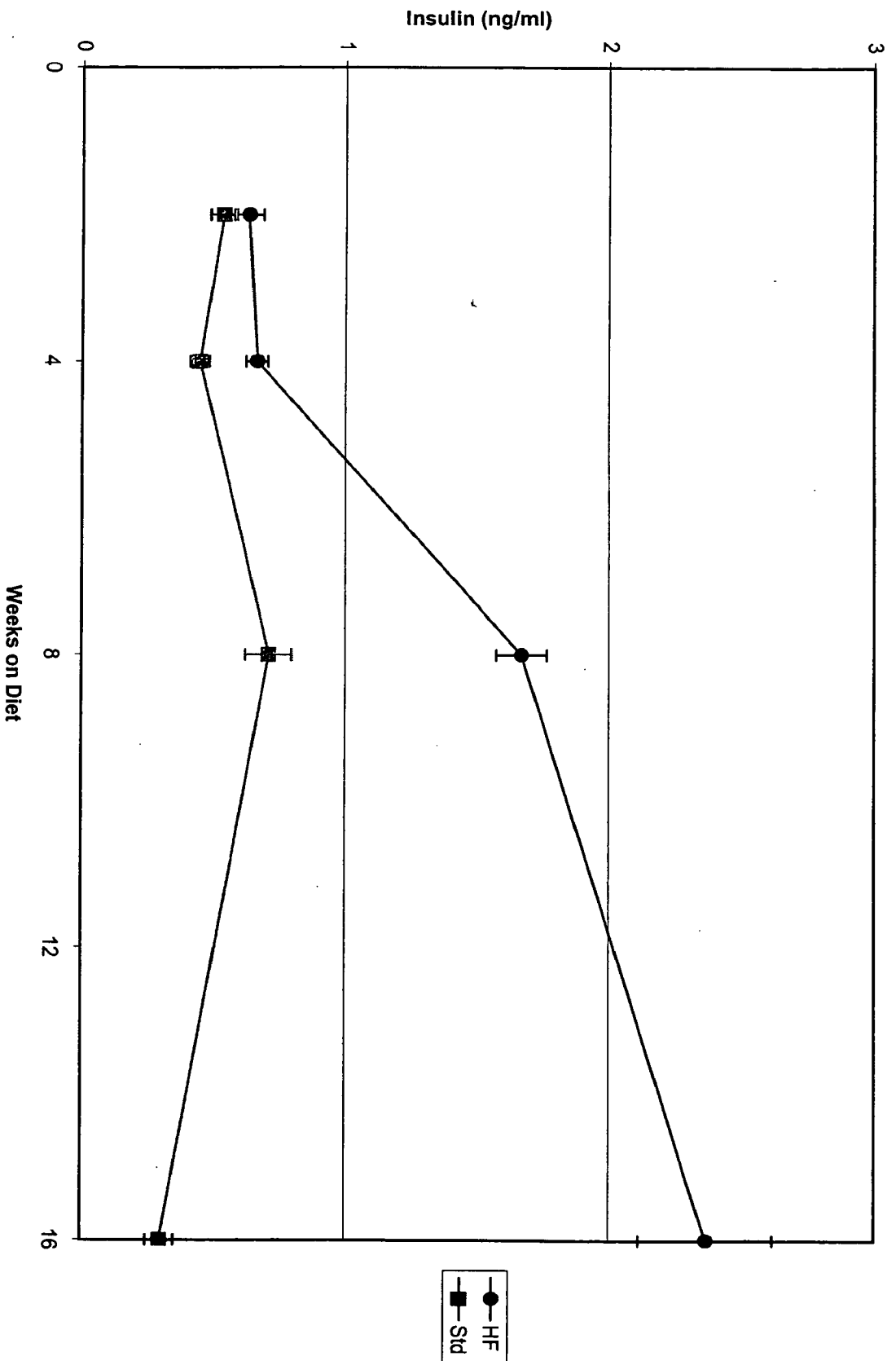


Figure 2

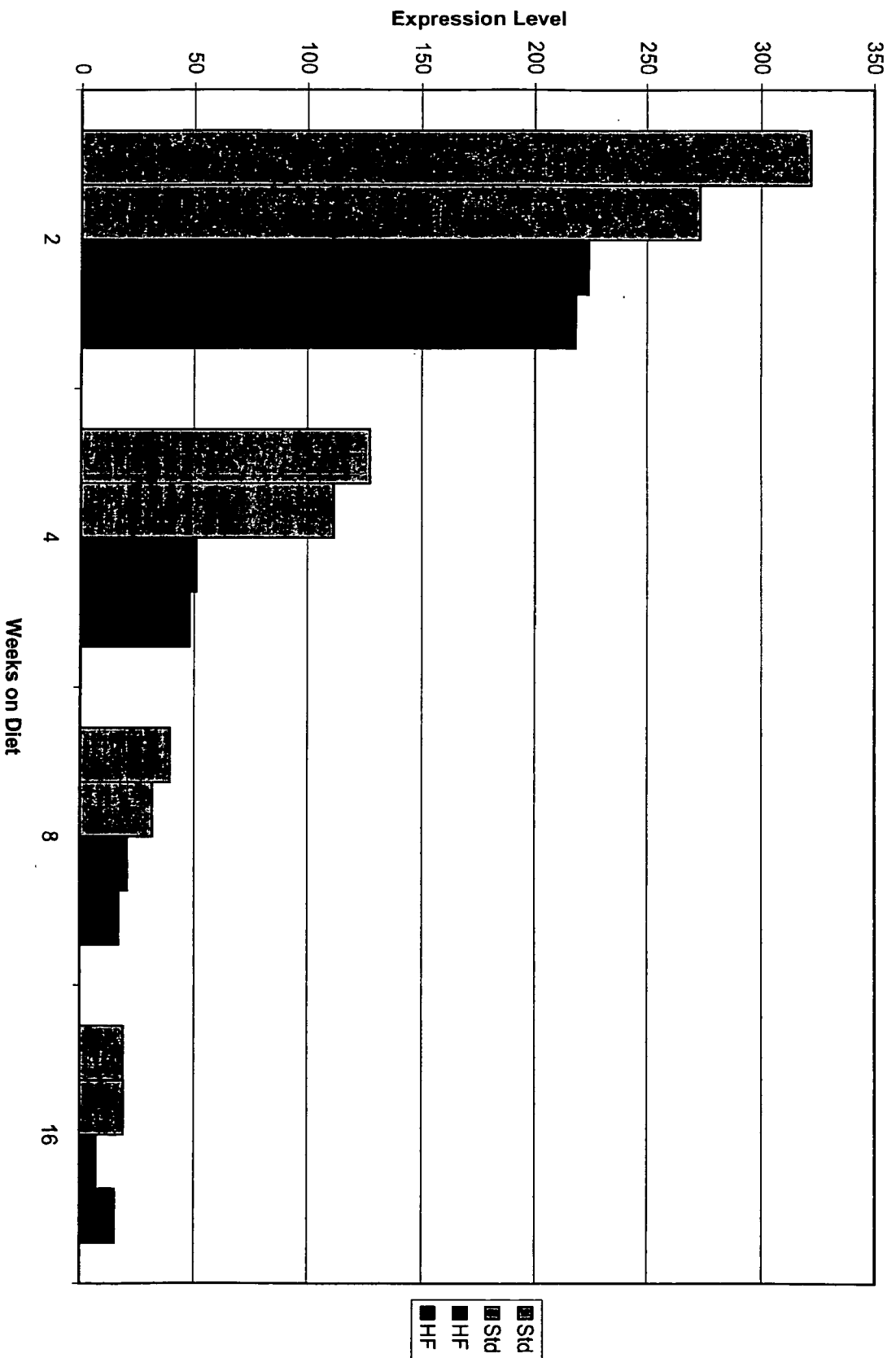




Figure 3(a)

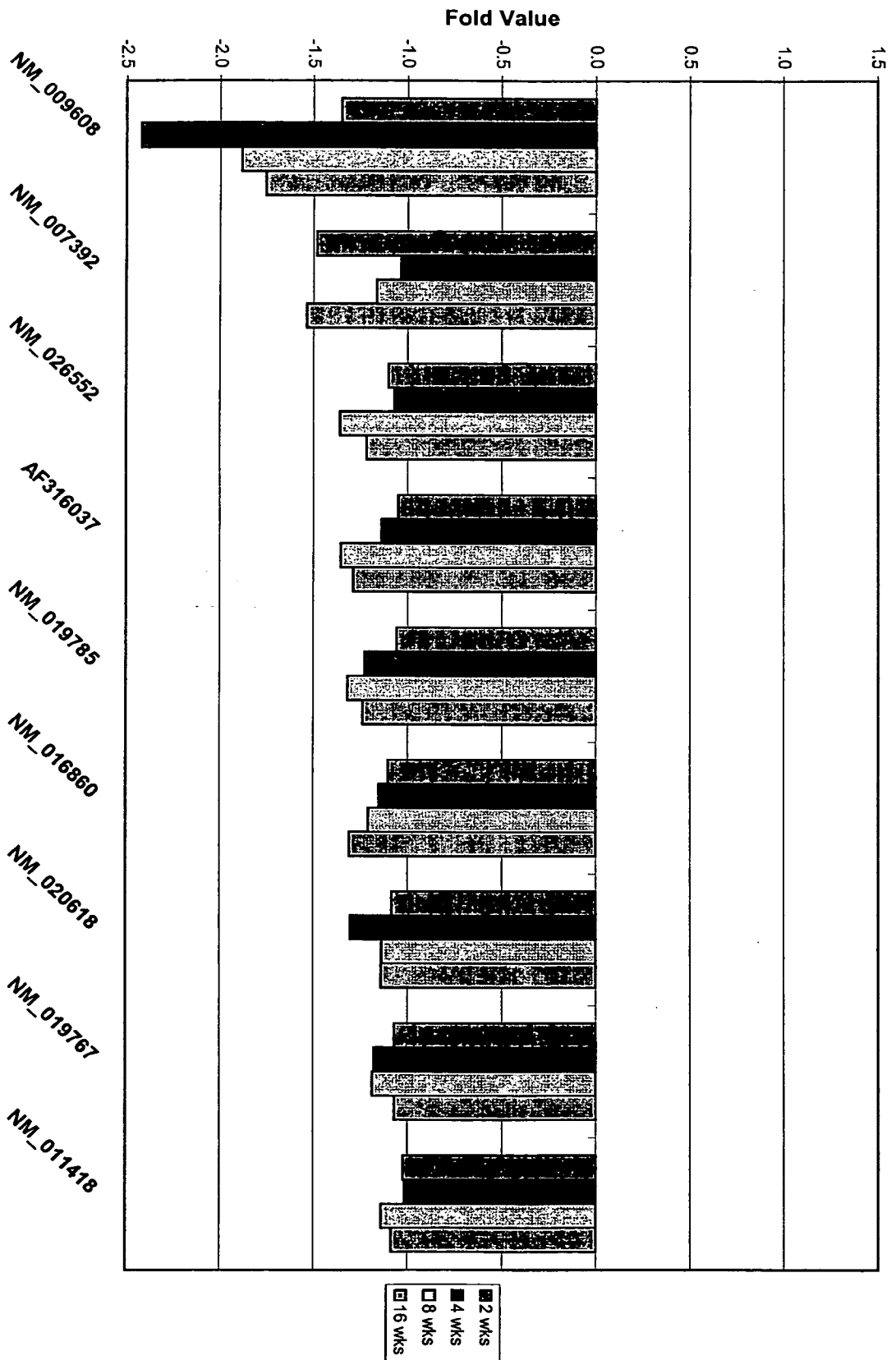


Figure 3(b)

